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Some Gynaecological Aspects of Referred Pain

BY

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IN this paper I propose to give a modified report of part of the work I published in 1941 in the form of a monograph.[1] Evidence will be adduced to support the view that pain can arise and be provoked in an abdominal organ, that this pain is independent of any involvement of the peritoneum or arteries, and may be abolished by anaesthetizing the area of skin to which it is referred. In order to explain these and other facts I suggested a new hypothesis. A more complete study of the wider problem of pain is afforded by Lewis[2] in his monograph published a year later, in which he gives a lucid and penetrating review of the literature, and incorporates the important contributions he made to this problem in association with Pickering, Pochin, Kellgren, and others. He arrived at a conclusion with regard to the central reference of referred pain which is not dissimilar to that I advanced.

Pain is a purely subjective, and consequently unmeasurable phenomenon which largely subserves a protective function. It is therefore not surprising that the great majority of sensory nerve endings are located in the skin, the protective covering of the body. All peripheral sensations may be ascribed to one of the four specific systems; touch, pain, warmth and cold, and while all sensory impressions reach the spinal cord through the posterior nerve roots, each system traverses a separate pathway to the sensorium.

The posterior root divides into a number of rootlets which enter the cord in the line of the postero-lateral sulcus, and then divide into medial and lateral filaments. The small fibres of the lateral filaments, which are thought to contain the pain-conveying fibres, pass into Lissauer's tract, where, after a short course, they end in the substantia gelatinosa of the posterior horn. New neurones, arising in this substance, cross the mid-line and travel in the spino-thalamic tract to end in the lateral nucleus of the thalamus. The fibres mediating temperature likewise cross to the opposite side shortly after entering the cord. It is

not yet determined whether pain has any true cortical representation, but it may be observed that there is no reason to suppose that direct stimulation of the cells of a pain apperception centre in the cortex, if it existed, would cause pain. We do know that section of the pain fibres running in the spinothalamic tract does not cause pain.

Superficial, or skin pain may be caused by pinching, and pricking, by adequate heat or cold stimuli, by electrical stimulation, and by other mechanical means, but rarely, and this is surely significant, without causing injury to cells. This is one feature which distinguishes superficial pain from tactile and thermal sensation. It is also possibly a feature which distinguishes it from some forms of visceral pain.

The threshold to pain may be lowered by both central and peripheral factors. A savage clearly feels pain less than a civilized man, and modern western civilization, with its restless bustle and noise, its anaesthetics and its aspirin, is responsible for a large and increasing number of people becoming hypersensitive to it in all its forms. Illness, overwork, worry, a vivid imagination linked with unhealthy anticipation, sleeplessness, dissipation of all kinds and the excessive intake of alcohol increase sensibility to pain, as do certain drugs. It is decreased by old age, loss of one or more of the senses, the attainment of mental equilibrium in association with physical fitness and by a considerable number of drugs. At rare intervals apparently normal individuals are encountered who are insensitive to most forms of pain, and are not even aware of discomfort when a tooth is extracted. Indeed, if reports can be believed, Cossacks and other peoples of Russia are almost incapable of feeling pain, as were the old guards who served under Napoleon.

Peripheral factors, such as a minor degree of local injury or an alteration in tension, such as may be effected by changing the position of a limb, may also alter the threshold to pain.

Lewis[2] has dealt exhaustively with the local factors associated with cutaneous hyperalgesia and hyperaesthesia. It is possible that a generalized cutaneous hyperaesthesia may be central in origin. After an attack of malaria I have found the whole of my skin, including the scalp, hyperaesthetic. While this condition lasted drops of water falling on the body from a shower bath caused an unpleasant sensation, as did the subsequent towelling if it was lightly done, and electrical stimuli, which were normally hardly appreciated, became distinctly painful.

Superficial pain is described as pricking, stabbing, or burning, and can be localized with great accuracy. Accuracy of localization is normally aided by the tactile sense, by vision and by experience. Pain arising in muscle, tendon, bone, periosteum, joint and other mesodermal structures is of a different quality and is often described as sickening. It may, indeed, cause emesis. Lewis points out that this type of pain may be caused by squeezing the web between two fingers. Visceral pain belongs to this deep type of pain although it is referred to the surface of the body. Pain cannot be measured, but it is possible to obtain evidence concerning its severity, quality, localization, duration, and its time-intensity curve. Pain is soon forgotten and the best evidence is therefore to be obtained in recurrent types of pain, or while the pain is actually being experienced.

Referred pain is pain which is appreciated at a point distant from the organ or structure in which it arises. The term was first used by Head[3] in 1893, in relation to pain arising in diseased viscera. Visceral pain has provided fascinating problems, provoked much discussion, and given rise to varied and mutually contradictory hypotheses, and for two main reasons. In the

first place it is known that the heart, lungs, liver, spleen, kidneys, stomach, gall-bladder and intestines are insensitive to stimuli which cause pain on the surface of the body.[4] Nevertheless we know that pain from the heart may be very severe, and be referred to the front of the chest, to the neck, and down the left arm; that appendicular pain may be appreciated just to the left of the mid-line, at or above the level of the umbilicus; that pain from the fundus of the bladder is referred to the lower abdomen while that from the trigone is referred to the tip of the penis; that pain from the ureter is referred down the right side of the abdomen and to the testicle of the same side; and that intestinal and renal colic are the most intense pains that man is called upon to endure. The first reason for confusion therefore, is that intense pain originates in structures that are insensitive to ordinary pain-producing stimuli.

The second reason is that the sympathetic nervous system has been accorded both an anatomical and a physiological connotation. The classical work of Langley and Gaskell has been so interpreted in physiological textbooks as to convey the impression that the sympathetic nervous system consists entirely of efferent nerves. These two physiologists concerned themselves solely with the motor effects produced by stimulation of sympathetic nerves, nevertheless the erroneous thesis, improperly attributed to them, dominated both physiology and medicine for well nigh a quarter of a century, and received clinical support from the studies of Lennander. This is all the more surprising when it is remembered that Sherrington was well aware of the fact that the sympathetic nervous system included sensory fibres, and that Dogiel had described sympathetic sensory proto-neurones in 1895.

The views ascribed to Langley and Gaskell were challenged and disproved by clinicians, notably by the French surgeon Leriche, on the following evidence. The smaller arteries are sensitive to puncture, and pain is usually felt when they are clamped or tied. The pain associated with Raynaud's disease and causalgia may be abolished in some cases by periarterial sympathectomy.[5] Jonnesco[6] and Ionescu[7] have found that the mechanical stimulation of both the cardiac nerves and the inferior cervical ganglion causes pain. Leriche and Fontaine[8] have caused pain in the jaw and behind the ear, by stimulating the superior cervical ganglion, notwithstanding the fact that the sympathetic chain above this level receives no white ramus and has generally been considered to be devoid of afferent fibres. Stimulation of the central end of the splanchnic nerve also causes severe pain.

In recent years the sensory side of the sympathetic nervous system has attracted the attention of physiologists, and in this country McSwiney and his fellow-workers have been the pioneers. Miller and Simpson,[8] and McSwiney and Suffolk,[9,10] have afforded physiological evidence which supports the view that afferent impulses from the viscera pass through the posterior nerve roots into the cord, the former workers using muscular reflexes, and the latter, dilatation of the pupil as their guide. It is therefore proved that the sympathetic nervous system includes sensory nerves, and almost certain that they enter through the posterior nerve roots into the cord, but nothing definite is known concerning their subsequent course in the spinal cord. The fact that double cordotomy affords immediate relief of pain to sufferers from malignant growths of the viscera, suggests that they travel with the somatic pain fibres in the spinothalamic tracts. Although the existence of these sensory nerves (which I shall refer to as "visceral-afferent nerves travelling in visceral-afferent pathways") has been recognized, the isolated

instances of pain caused in viscera by surgical interference (such as that caused by the tip of the ureteric catheter when it is pressed against the wall of a renal calyx) have hitherto not sufficed to disprove the contentions of Lennander.

Bearing these considerations in mind it is easy to trace and to understand the reasons for the varied and mutually exclusive hypotheses which have been advanced to explain visceral pain. Although Hunter recorded that an animal could eat its food with relish while its viscera were being burned, it was not until 1883 that Sturge[11] made the first attempt to explain referred pain. Puzzled by the reference of cardiac pain to the left arm he came to realize that the "region of the spinal cord which gives origin to the brachial plexus gives origin also to the greater part of the fibres which eventually find their way to the heart." He came to think of a small area of commotion occurring in the cord, which was extended by the mediation of commisural interpolar fibres, which connect the cells one with another, and suggested the analogy of epilepsy, which was striking, if not altogether convincing. Sturge therefore postulated a true visceral or "splanchnic" pain, and a pain which was referred from the viscus in the manner outlined above. Ross[12] accepted these ideas.

Lennander,[4] however, after very thorough investigations, concluded that all the abdominal viscera were insensitive to burning, cutting, squeezing and other noxious stimuli, and that consequently no pain could arise in them. He postulated the more simple explanation that the sensation of pain associated with disease of the abdominal viscera arose in the peritoneum, its sub-serous coat, and, when inflammation was present, in the root of the mesentery; all these structures being supplied by somatic nerves. Mackenzie,[13, 14, 15] was convinced by Lennander's evidence concerning the insensitivity of the abdominal viscera, but was equally impressed by the reference of cardiac and appendicular pain. He was therefore driven to assume that the ordinary non-painful stimuli from the viscera could, when quantitatively increased, set up a focus of irritation in a segment of the spinal cord and thus indirectly stimulate sensory nerves. The pain so caused was referred to the cutaneous areas supplied by those nerves. Mackenzie, Ross, and Sturge, as I understand them, believed the sensory nerves to be stimulated proximal to their endings. According to this view local anaesthetization of the cutaneous areas involved could have no effect on the pain.

More recently Morley[16] has supported the underlying conception of Lennander's hypothesis, although he believes in the existence of a true visceral or "splanchnic" pain. He affirms that both referred pain and abdominal rigidity arise as the result of irritation of the somatic nerves which supply the parietal peritoneum, which he postulates to be very sensitive. He found, during the course of operations under local anaesthesia, that irritation of the diaphragmatic peritoneum with gauze caused shoulder pain on the same side, and that this pain could be abolished, or significantly lessened, by anaesthetizing the skin of the area to which it was referred. Escaped blood from an ectopic gestation causes shoulder pain, as may the CO_2 used for the insufflation of the Fallopian tubes. The diaphragmatic peritoneum is indubitably very sensitive, even to gas, but there is no justification for Morley's assumption that the rest of the parietal peritoneum is equally sensitive. Indeed, other observers have reported that the parietal peritoneum is insensitive to all forms of sensory stimuli. Woolard, Roberts and Carmichael[17] subsequently reported that direct stimulation of the phrenic nerve by pinching caused

severe shoulder pain, and that the previous anaesthetization of the cutaneous area to which it was referred in no way affected the character, or lessened the intensity of the pain. These authors do not indicate very clearly what steps they took to ensure cutaneous anaesthesia of the shoulder area, or what success they achieved. Nevertheless, the divergence between the results obtained by Morley on the one hand, and Woolard, Roberts and Carmichael on the other, does not necessarily diminish their significance, for it could reasonably be attributed to the difference in the intensity of the stimulus they severally applied.

Hurst[18] came to believe in a true visceral tenderness, and concluded from X-ray examinations that the gastric ulcer is as a rule the seat of localized tenderness, and that the point of actual tenderness changes with alteration in the position of the ulcer occasioned by altered posture. Morley and Twining[16] confirmed Hurst's findings, but drew therefrom quite different conclusions. Whereas Hurst believed the ulcer itself to be tender, the former workers hold the parietal peritoneum covering the ulcer to be the seat of the tenderness.

In an attempt to explain the insensitivity of the viscera to stimuli which cause pain on the surface of the body, Hurst suggested that just as the ear was insensitive to light, and the eye to sound, so the intestines were insensitive to cutting, pinching, or burning, but that they were sensitive to stimuli which caused increased tension in their musculature. This conception of an adequate stimulus has proved valuable, but the form in which it was expressed offers grounds for criticism. Sensory nerves are all much alike and vary only with regard to the speed with which they conduct impulses, a variation which may possibly be correlated with the area of cross section. It is the nerve endings which are of real significance, those at the periphery being designed to collect stimuli of a certain nature, while those at the centre are responsible for their interpretation. A nerve fibre which conducts the sensation of cold can be stimulated by heat, but the sensation appreciated will be that of cold.

Finally, it may be recorded that Weiss and Davies[19] concluded that the direct stimulation of a viscus without affecting other structures, was beyond the bounds of possibility. They therefore attacked the problem indirectly, and assumed the possibility that a focus of irritation was caused in a segment of the cord by the "bombardment" of non-painful stimuli from the diseased viscus, and that the normal stream of impulses from the cutaneous areas to which the pain was referred, were rendered painful when they entered this focus of irritation. They found that anaesthetization of the cutaneous areas to which the pain was referred abolished visceral pain, and concluded that this observation supported Mackenzie's hypothesis.

It is my contention that the gynaecologist enjoys unique opportunities for studying the problem of referred pain. All are agreed that the uterus is an abdominal viscus innervated in the same way as are the other abdominal viscera. More than half the women in Europe, America, and Australia suffer, or have suffered from some degree of pain at monthly intervals. Dysmenorrhoea occurs in perfectly healthy women, and with such regularity that they are able to record their sensations with precision. The pangs of childbirth, in some degree or another, accompany the birth of nearly every child. Thus, concerning no other type of pain is there anything approaching the wealth and completeness of the clinical data, as that which has accumulated from all civilized countries on the subject of uterine pain.

The uterus is not so insensitive to ordinary painful stimuli as is commonly

asserted, and it seems to me that gynaecologists have been unduly influenced by the oft-repeated assertions of the insensitivity of the viscera. It is true that the fundus uteri may be painlessly incised, but it is not true that the volsellum may be painlessly applied to the lip of the cervix. Most women dislike the application of this instrument, and although the stab of pain is shortlived it is none the less unpleasant. Removal of a piece of tissue from the external os uteri, whether with scalpel or scissors, causes considerable pain, as does the insertion of a ligature to control haemorrhage. The neighbourhood of the internal os is often sensitive to a probe, and it is rarely possible to curette the uterus, however gently the operation be performed, without causing quite severe pain. Further, cervicitis often causes movement of the cervix in any direction to be painful.

These clinical observations are very valuable, but the most important fact is that uterine pain, in no way differing from dysmenorrhoea, or the pains of labour, may be occasioned by a simple procedure. Some 10 years ago[20] I began to treat endocervicitis by the application of a stick of silver nitrate, and this method of treatment unexpectedly afforded a simple means of provoking and studying pain referred from the cervix and the body of the uterus.

It is therefore proposed to consider this problem in two parts.

(1) Uterine Pain.

(*a*) As it occurs in normal healthy women, namely dysmenorrhoea.

(*b*) As provoked by the application of a stick of silver nitrate to the cervical mucosa and endometrium.

(*c*) As it occurs during labour. Observations on the relief of these pains by local anaesthesia will be recorded.

(2) Observations on the Viscero-motor Reflex.

PART I.

Dysmenorrhoea.

In England, menstruation most commonly commences during the 14th and 15th years of life, and it is probable that the menarche occurs either before or after that period of life in less than 15 per cent of girls.[21] At their onset the menses are often irregular, and the interval between the first and second period may exceed a year. The first period is rarely, if ever, painful and it is only after the lapse of one or more years that pain becomes to be associated with the flow. In some of the worst cases of dysmenorrhoea the history of freedom from any menstrual pain for some years after the onset of the menarche is frequently elicited. It may, therefore, reasonably be concluded that the pain is not caused by, or even associated with, structural defects in the uterus.

The pain may commence some hours before the flow, or may not occur until it becomes established. It may last a few hours or may persist for two days or longer. It is usually described as being cramp-like rather than continuous. The pain may be very mild, causing less discomfort than a purgative, while it may be as intense as that normally experienced during labour, and may be associated with pyrexia, a leucocytosis, and even with jaundice. It cannot be attributed to inability of the blood to escape from the uterus, for it is always possible to pass a small metal cannula into the uterine cavity. The pain is most commonly referred to the lower abdomen, but sometimes to the lower part of the back, or over the hips, and still less commonly down the upper third of the insides of both thighs. The pain of dysmenorrhoea may usually, if not invariably, be abolished by anaesthetizing the areas of skin to which it is referred.

In England a small percentage of girls

and women invariably suffer intense pain with each period. They faint, vomit, and have to go to bed, and those who have to earn their living thereby stand in jeopardy of losing their employment. At the other extreme some 20 per cent of women never suffer a twinge of pain or discomfort during menstruation. In between these extremes lies the great majority of women. The pain is usually tolerable and does not interfere with their work or play, but should they do too much, become over-excited, lead irregular lives, or become run down through over-study or any other cause, it becomes severe.

I have found in all cases of dysmenorrhoea that deep palpation over the tip of the left transverse process of the second lumbar vertebra, the point of emergence of the first lumbar nerve, causes pain. The patient may also be sensitive to pressure over the corresponding position on the right side, but in my experience the tenderness is usually either limited to, or more marked on the left side. I have no explanation to offer for this phenomenon, but think it possible that dysmenorrhoea may sometimes be causally related with a slight departure from the structural integrity of the spinal column, of insufficient magnitude to be detected by radiological investigation. This deep tenderness may also be elicited not infrequently in patients suffering from chronic ovarian pain.

The most fascinating and illuminating facet of the problem of dysmenorrhoea is its indivisibility from psychological factors. It not infrequently happens that women who invariably suffer intense menstrual pain enjoy absolutely painless periods when brought into hospital for investigation. The onset of dysmenorrhoea is often associated with a change of work or of environment. In Bangkok there were two large mission schools for girls. In the one, approximately 80 per cent of the girls went to bed for the first day of the period, whereas in the other less than 20 per cent felt the necessity even to lie down for a while. The class of girl was the same, but the traditions differed. It sometimes happens that a girl ceases to suffer from dysmenorrhoea when she falls in love, and before indulging in sexual congress. Further, this is probably the only type of severe pain which may be relieved by a small amount of whisky or gin.

Primary dysmenorrhoea is almost invariably cured by childbirth, and any subsequent pain is due to chronic infection. It may likewise be cured for a time, if not permanently, by dilating the cervix and incising the "internal sphincter," or by applying the silver stick to the cervical mucosa, although it is of interest to note that the first period subsequent to these operations may be painful. Other means have been successfully employed in the treatment of dysmenorrhoea, amongst which may be mentioned psychotherapy, hypnotism, spinal manipulation, and hormone therapy.

It would therefore seem evident that primary dysmenorrhoea is as independent of structural defects in the uterus as it is dependent, directly or indirectly, on psychological factors. This does not mean that the pain experienced is not very real, and even intense. This aspect of the problem will be discussed later, but it may here be instanced that the pain of dyspareunia, associated with spasm of the introitus, may be very severe notwithstanding the fact that it can as a rule be easily abolished by simple psychological treatment.

The Results Obtained by the Application of a Stick of Silver Nitrate to the Cervical Mucosa.

More than 10 years ago I began to treat the endocervicitis so frequently encoun-

tered in the postnatal department by the application of a stick of silver nitrate to the cervical mucosa. The treatment was simple, rapid, painless and reasonably efficacious. Some time later I used the same treatment in the gynaecological out-patient department and was more than surprised to find that it not infrequently caused pain.

Silver nitrate. Salts of heavy metals when applied to mucous membrane precipitate the proteins with which the metals form a complicated adsorption complex. If this adsorption complex is soluble in the acid which is liberated, the metal penetrates deeply into the cells, causing a corrosive action. In the case of silver nitrate the reactions are affected by the formation of silver chloride, but the protein complex is soluble in the excess of nitric acid so that the metal penetrates the tissues deeply.

It is not possible to state to what extent the corrosive action of silver nitrate is to be attributed to the liberated nitric acid, but suitably treated sections demonstrate that the silver penetrates the whole depth of the mucosa, and in particular stains the endothelium lining the blood-vessels. The standard stick used measured 6 cm. in length and has a diameter of 0.5 cm.

The Method of Applying Silver Nitrate.

After the introduction of a Sim's speculum, the anterior lip of the cervix was grasped with a volsellum, and the silver stick was introduced through the external os uteri with a suitable pair of forceps, and then pushed up the canal until the internal os was reached. Except in postnatal patients the silver stick could not at first be introduced through the internal os, because the upper part of the cervix contracted and tended to expel the stick with some force from the canal. If, however, the stick was held in position by the forceps the spasm disappeared in about 30 seconds. Once the spasm had passed away the stick would lie in the canal, and might pass into the uterine cavity, and only with difficulty be recovered. It was moved up and down against the walls of the cervix for some 2 minutes, after which time it was usually reduced in size by one half. The stick having been withdrawn, the vagina was plugged with gauze soaked in glycerine to prevent the vagina and perineum from being burned.

Pain.

It is clearly impossible to treat the endometrium with the silver stick without concomitantly affecting the cervical mucosa and for this reason my remarks will be confined to the treatment of the cervical mucosa and of the endometrium in close juxtaposition to the internal os. I would observe, nevertheless, that there is every reason to suppose that the endometrium is as sensitive to the silver stick as is the cervical mucosa. I have already stated that this treatment, except in the postnatal department, frequently caused pain, sometimes of a severe nature. It can be asserted that every woman who suffers from primary, or any other form of dysmenorrhoea will suffer pain as a result of this treatment, and that the pain will be identical with the pain that she suffers during her period, although it may be more severe. With other patients it is not possible to prognosticate whether the treatment will cause pain, but there are three factors which are of significance: (*a*) the degree of dilatation of the internal os uteri; (*b*) the social status of the patient, and (*c*) the thickness of the cervical mucosa.

The degree of dilatation of the internal os uteri. Although there would appear to be no anatomical muscular[22] ring at the level of the internal os uteri, clinical evidence

indubitably proves that there is a powerful sphincter closing the cavity of the uterus from the cervical canal. Any effort to stretch this sphincter causes immediate pain. In nulliparae the region of the internal os is particularly sensitive to the silver stick, and if the sphincter be tightly closed it may be opined that the patient will subsequently suffer some degree of pain.

The social status of the patient. The difference in the incidence of pain subsequent to this manoeuvre between the hospital and the higher class of patient is very marked. In my experience every patient of the upper middle class tends to suffer considerable pain as the result of this treatment, which must therefore be carried out under some form of anaesthesia.

The thickness of the cervical mucosa. The shrinkage of the silver stick, and consequently the amount of free silver liberated, is largely dependent on the amount of available fluid, which in turn is determined by the thickness of the mucosa and the amount of secretion present. If treatment be carried out shortly before a period is due the pain will be more severe and likely to last several days. Subsequent menstruation, if it occurs within 48 hours of the application, will be painful even if the individual normally experiences no pain at that time.

The Onset of the Pain.

In the majority of patients the onset of the pain occurred within 2 minutes of the application of the silver stick. In 2 patients the external os uteri itself was unduly sensitive and marked pain referred to the lower abdomen was appreciated immediately it was touched by the silver stick. It is not very uncommon to encounter patches of erosion on the external os which when touched either by the silver stick, or by cotton wool dipped in pure lactic acid, give rise to a sharp stab of pain referred to one or other side of the lower abdomen. The application of the volsellum to the anterior lip of the cervix may likewise give rise to a similar transient stab of pain. The onset of pain was frequently delayed for 10 minutes, and in one case for as long as 4 hours. The second and third applications of the silver stick were usually accompanied by a diminishing degree of pain.

The Site of the Pain.

In the case of nearly every patient who experienced pain it commenced, somewhat surprisingly, in the middle line, usually at a point about one third of the distance from the symphysis pubis to the umbilicus. From there it radiated across the lower abdomen, so that the whole area below a line drawn between the two anterior superior iliac spines was involved. The pain was commonly localized to this area, but 3 other sites were not infrequently involved: (*a*) the back; (*b*) over the iliac crest on either side, about a third of the distance from the anterior superior iliac spine to the vertebral column, and (*c*) down the inner sides of the thighs reaching for about a third of the distance to the knees. (See Figs. 1 and 2).

These are the identical areas to which both labour pains and the pain of dysmenorrhoea are referred, and the skin covering these areas is supplied by branches of the 1st lumbar nerve. Three different methods have been used for delimiting dermatomes. Sherrington,[23] working with monkeys, cut a number of posterior nerve roots leaving but one isolated root intact, and subsequently investigated the responses to painful cutaneous stimuli. Foerster[24] found surgical reasons for adopting the same technique in man. Head[25] mapped out the dermatomes by studying the cutaneous eruptions of herpes zoster and

it is interesting to note that his margins are contiguous and not overlapping as were those noted by Sherrington. Kellgren[26] mapped the dermatomes of the body by injecting hypertonic saline solution into muscles and into the deep interspinous

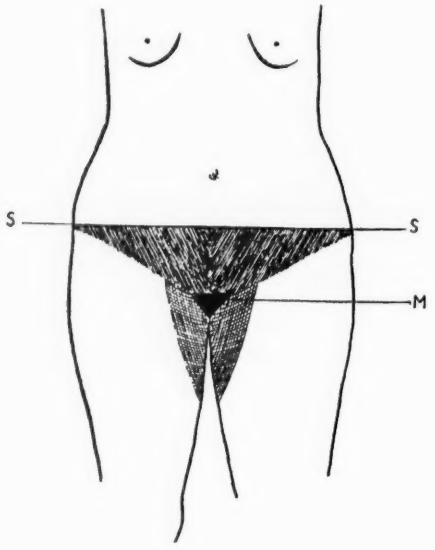

FIG. 1.

S=anterior superior iliac spine; M=mons veneris. The shaded regions indicate the cutaneous areas on the anterior surface of the body to which uterine pain is referred. These areas are supplied by branches of the first lumbar nerve.

ligaments of the vertebral column. So far as I am aware this is the first occasion that the first lumbar dermatome, or any other, has been determined by direct stimulation of a viscus. (Compare Figs. 1, 2, 3 and 4). It may here be noted that in certain cases in which one or other ovary was tender, and the site of chronic ovarian pain, the silver stick applied to the cervical mucosa resulted in pain which was more or less localized to the lower abdomen of the affected side, and it frequently happened that this treatment permanently cured the condition.

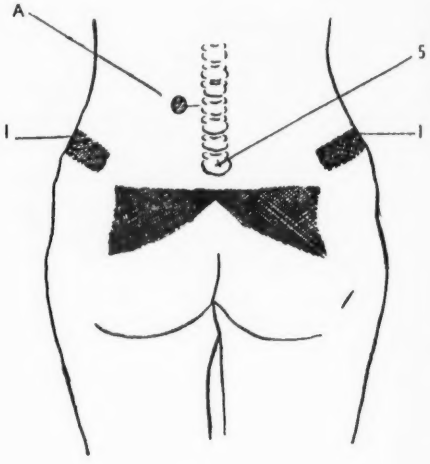

FIG. 2.

I=level of iliac crest; A=the tip of the left transverse process of the second lumbar vertebra; the numeral 5 denotes the spine of the fifth lumbar vertebra. A is the point of emergence of the left first lumbar nerve and this area is usually tender to deep pressure in women who suffer from dysmenorrhoea. The other shaded regions indicate the cutaneous areas on the posterior surface of the body to which uterine pain is referred, i.e. the hips and the back. These areas are supplied by branches of the first lumbar nerve.

The Intensity of Pain.

In some cases the pain caused was intense and more severe than that associated with dysmenorrhoea. The only drug which afforded relief in such cases was morphia, although aspirin was usually reasonably efficacious.

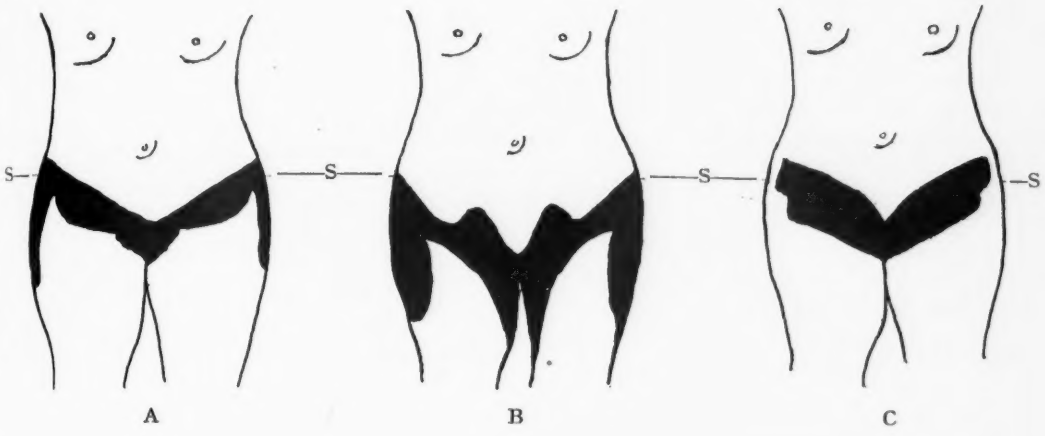

FIG. 3.

The ventral distribution of the first lumbar dermatome: A according to Foerster; B according to Head; and C according to Kellgren. These authors attempted to demarcate all the dermatomes of the body, and it is not easy to be sure of the exact boundaries they intended for any single dermatome. S = Ant. Sup. Iliac Spine.

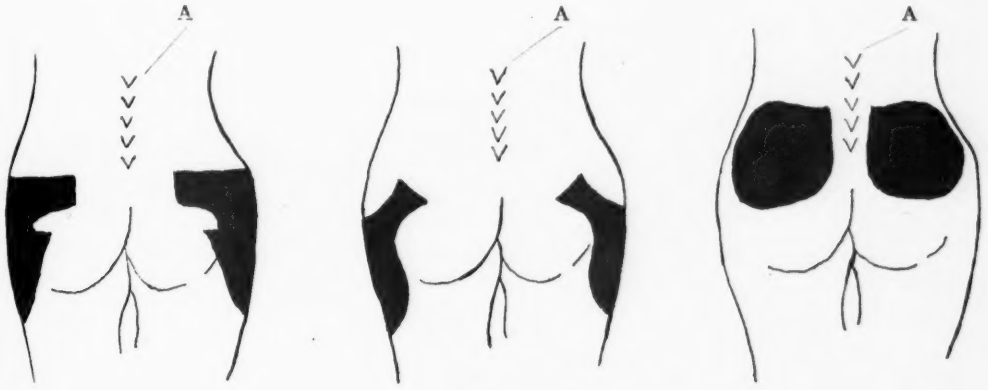

FIG. 4.

The dorsal distribution of the first lumbar dermatome: A according to Foerster; B according to Head; and C according to Kellgren. A denotes lumbar spine.

Cutaneous Hyperalgesia and Hyperaesthesia.

The pain referred to the lower abdomen was frequently associated with an apparent hyperalgesia of the skin, but the severity of the pain made it difficult to make any satisfactory observations. Stroking the affected skin lightly with the finger, or with cotton wool, was considered definitely unpleasant and was sometimes described as painful. It was not found possible to come to any conclusion with regard to any altered perception of heat or cold but in some cases there appeared to be a heightened perception to cold. It can, however, be asserted with confidence that any alteration which may have occurred in cutaneous sensibility disappeared with, and did not outlast the uterine pain.

The Prevention of Pain

It was sometimes found possible to prevent all pain by previously infiltrating the cervical mucosa at the level of the internal os with a 1 per cent solution of novocain, but not always. The discrepancy in the results may possibly be attributable to the fact that the procedure presented considerable technical difficulties. On the other hand it was not found possible on any single occasion to relieve the pain by this procedure after the silver stick had been applied. It is a remarkable fact that if the silver stick be applied while the patient is under a general anaesthetic the subsequent pain is negligible. This is all the more remarkable as the treatment is usually finished before the pain commences. The significance of this observation will be discussed later.

The Relief of Pain Caused by the Application of the Silver Stick.

It has already been stated that the pain caused by this procedure can usually be relieved by aspirin, although it may sometimes be necessary to resort to morphia. It is a somewhat surprising fact that in many cases considerable relief of pain was afforded by removing the vaginal plug, seeing that the sensory supply of the vagina derives from sacral nerves. The pain over the iliac crests could easily be abolished by infiltrating the subcutaneous tissues at the points where the nerves (branches of the 1st lumbar nerve) pass in close relation to the bone. The abdominal pain could usually, but by no means always, be completely relieved for a time by infiltrating the ilio-hypogastric and ilio-inguinal nerves where they pass in close relation to the anterior superior iliac spines, and as a rule the injection of some 10 c.cm. of a 2 per cent solution on either side sufficed. The relief so occasioned lasts for less than one hour, although similar injections relieve the abdominal pain of dysmenorrhoea for several hours, if not completely. The relatively short time of immunity from pain thus procured in these patients may find its explanation in the fact that the pain is continuous, whereas in dysmenorrhoea it is spasmodic. I suggest that the differences encountered in the alleviation of the abdominal pain associated with dysmenorrhoea and that associated with the application of the silver stick to the cervical mucosa has an explanation similar to that already suggested for the divergence in the results recorded by Morley[16] on the one hand, and Woolard, Roberts and Carmichael[17] on the other.

The pain following the application of the silver stick to the cervical mucosa was so strikingly consistent in regard to its onset and distribution that it is not proposed to report cases in detail. A table (Table I) is, however, appended which shows the results obtained in 41 consecutive patients so treated in a gynaecological out-patient department in London, most of whom were in the third decade of life. Only 5 of these

patients came for treatment solely because of dysmenorrhoea, but the majority of women in group 2 suffered from painful menstruation in addition to abdominal pain. It may be recorded that 5 out of the 12 women in this group experienced the most severe pain subsequent to the treatment over one or other ovary. It is also of interest to note that this procedure so frequently caused vomiting, because, except in isolated instances, the pain was not severe. It will be recalled that the 2nd stage of labour is frequently ushered in by emesis. Visceral pain clearly belongs to the deep type of pain.

TABLE I.

Condition treated	No. of patients	No. who felt pain	Site of pain			Severe pain	Vomited
			Abdo.	Back	Hips		
Group 1. Dysmenorrhoea	5	5	4	3	0	4	3
Group 2. Chronic salpingitis and salpingo-öophoritis	12	11	10	4	1	6	5
Group 3. Leucorrhoea, and cervical erosion	21	7	7	2	0	1	1
Group 4. Arthritis	3	2	2	0	0	1	1

THERAPEUTIC RESULTS.

This is a convenient point at which to make a brief digression in order to evaluate the therapeutic results of this treatment. Young[27] has been the chief exponent in this country of the view that chronic cervicitis may cause pain in the pelvis and lower abdomen, dyspareunia, bladder and menstrual troubles, together with a disturbance of the general health manifested by such symptoms as undue fatigue, headache, arthritis and cardio-vascular disturbances. Cervicitis is easily provoked but with difficulty cured. The intractibility of the condition is due to the natural crypts and crevices which occur in the cervical mucosa no less than to the racemose structure of the cervical glands. Infection tends to become locked up in the recesses of the glands in the deeper layers of the cervix, while the consequent swelling of the tissues militates against drainage.

The diagnosis of the condition can be made with ease, and I will quote from his paper: "If the examining fingers are placed on the cervix and this be moved laterally, antero-posteriorly, and upwards, it is found that in health a considerable amplitude of displacement can be obtained in all these directions, and that even at its maximum this displacement is painless. In cases of cervicitis, on the other hand, this mobility is commonly restricted, and in those cases in which pain is present any attempt to displace the cervix at once provokes the symptom in the location in which it has been complained of by the patient, be it in the iliac fossa, the back, or the bowel." I confess that for many years I considered these claims excessive, and for two main reasons. In the first place I did not believe that such pain could arise in the cervix, and in the second I considered

his arguments vitiated by the fact that obvious cervicitis so commonly occurred without causing any symptoms other than leucorrhoea. I am now satisfied that pain of a severe nature can arise in the cervix, and that the same stimulus can provoke pain in some women and none in others, and can therefore confirm Young's main, and very important contentions.

The symptoms he, and others describe can clearly be attributed to three main factors: (*a*) toxaemic absorption, (*b*) local extension of infection, and (*c*) referred pain.

Toxaemic absorption. It is recognized that arthritis can arise from a gonococcal infection of the cervix and be cured by treatment limited to the cervix. I am satisfied that other forms of arthritis, no less than the other disturbances of the general health above enumerated, can arise from a chronic infection of the cervix. Indeed, there is reason to suppose that chronic cervicitis is the most potent source of chronic infection in a woman.

Local extension of infection. Cervicitis may be primary, and extend through the parametric tissues to involve the pelvic colon, bladder[28] and ovaries. Conversely, it may represent an extension, and one of the late sequelae of a generalized pelvic infection. In either case it is easy to understand how such symptoms as dyspareunia, polyuria, and pain associated with the large bowel could arise.

Referred pain. The problem which is particularly relevant to this study, and peculiarly difficult to elucidate, is to what degree the symptoms associated with cervicitis can be attributed to irritation of the cervical nerves. Discussion will here be limited to bladder symptoms. It is beyond dispute that some cases of frequency may be cured by treatment confined to the cervix. Such treatment might indirectly clear up any extension of infection from the cervix to the base of the bladder. There is, nevertheless, some evidence which suggests that this simple explanation does not represent the whole truth. In the first place amelioration of the bladder symptoms may occur long before the cervicitis is cured, and without any change in the urine, which may contain as many pus cells after the symptoms have cleared up as it did before the treatment was commenced. In the second place the trigone of the bladder is in closest proximity to the cervix, and pain from this part of the bladder is not referred to the suprapubic region. Further, we know that painful haemorrhoids, and haemorrhoids which have been injected, sometimes cause frequency of micturition, and it must be assumed that this symptom so caused represents a "nervous" phenomenon, notwithstanding the fact that pain from haemorrhoids is conveyed by sacral nerves. For these reasons I think it not improbable that frequency of micturition may result from irritation of cervical nerves. This conclusion is strengthened by the fact that chronic ovarian pain may sometimes be cured by the application of the silver stick to an apparently healthy cervical mucosa.

Most authorities are content to treat cervicitis, after the canal has been dilated, with three sweeps of the thermocautery. The advantage of the method I have advocated lies in the fact that the whole of the mucosa is treated, most of which comes away in a cone-shaped "silver slough" some 3 to 5 days later. The treatment itself is not painful, but the subsequent pain demands either that it be carried out under anaesthesia or that adequate analgesic drugs be given.

The Relief of Labour Pains by Local Anaesthesia.

Apart from the pain occasioned by the stretching of the vagina and vulva, the

pangs of childbirth differ in no way from dysmenorrhoea, except in degree. Low spinal anaesthesia, adequate for operations on the vagina, cervix and rectum, affords no obvious relief to a woman in the 2nd stage of labour, although the pain occasioned by the stretching of the vagina is abolished. On the other hand, the pain associated with the 1st stage of labour may be banished merely by anaesthetizing the skin of the lower abdomen. If at this time the ilio-hypogastric and ilio-inguinal nerves are infiltrated with an adequate amount of a suitable solution of some local anaesthetic as they pass in close relation to the right anterior superior iliac spine, all the pain associated with uterine contractions immediately disappears from the right side of the abdomen. This result I found invariable. If now the corresponding nerves on the left side be similarly anaesthetized, it frequently happens that pain over the iliac crests, hitherto unappreciated, becomes severe. The nerves concerned, as has already been stated, can be easily anaesthetized, and then, curiously enough, pain in the region of the mons veneris and the inguinal canals may be appreciated. It is remarkably easy to abolish pain from one side of the abdomen and from the iliac crests, but it is extremely difficult to eliminate all abdominal pain associated with the uterine contractions. It would seem evident that if pain referred to the distribution of one set of fibres is abolished, it is appreciated in undiminished intensity in areas, hitherto painless, which are supplied by nerves which have not been anaesthetized. Unless all the nerves concerned are anaesthetized the woman is not conscious of much relief of pain.

A similar experience is encountered when attempts are made to treat chronic shoulder pain by the injection of a local anaesthetic. It has already been stated that a woman in the 2nd stage of labour experiences little, if any relief of pain from a low spinal anaesthetic. In any given individual the sum total of pain at any given stage of labour would appear to be fairly constant, and the relief of one area concerned accentuates the pain referred to others. The converse of this law is demonstrated by the relief afforded by the application of a mustard plaster in the treatment of localized pain.

I have many times succeeded in abolishing all pain, but if this is effected too early the patient goes out of labour. On only 2 occasions have I succeeded, by a combination of the local anaesthesia here described, together with blocking the pudendal nerves in the ischio-rectal fossa, in rendering both the 2nd stage of labour and delivery absolutely painless. This form of anaesthesia during childbirth probably has no wide application, but the most successful results are likely to follow blocking the first lumbar nerve as it emerges on either side, together with both pudendal nerves.

Part II

The Viscero-Motor Reflex.

Mackenzie postulated that an irritable focus in the spinal cord, occasioned by afferent visceral stimuli, stimulated not only the sensory but also the motor nerves of the same segment. This he regarded as a protective mechanism. We may consider the implication of this hypothesis in relation to uterine pain. He assumed[14, 15] that the stream of non-painful impulses travelling in the sympathetic pathways reaches "the pain scheme" (in the spinal cord) "at the synapses X, where the cerebrospinal and autonomic nerves meet." "The abnormal stimulus spreads beyond the sympathetic centre" (in the

posterior horn of the first lumbar segment) "and affects nerve cells in its immediate neighbourhood. The cells so stimulated react according to their function . . . the motor producing contraction of muscle." Now it is obvious that there are no motor cells in the posterior horn of the first lumbar segment, and it is a fact that contraction of the abdominal musculature is almost entirely affected by the lower intercostal nerves. We will however assume that Mackenzie had in mind a reflex effected by intercommunicating fibres in the cord for which experimental proof has been reported.

Miller and Simpson[8] have caused contraction of the abdominal musculature, and movements of the hind legs in decapitated cats by centripetal stimulation of the mesenteric nerves, and also by traction on the stomach or its mesentery. McSwiney and Downman[29] have obtained similar results by pinching the duodenum or the head of the pancreas, and also by scraping or heating the serous coat of the gut. They found that the viscero-motor responses sometimes deteriorated to extinction without noticeable change occurring in the general reflex activity of the limbs. Lewis and Kellgren[30] obtained the above responses by pinching the pancreas.

Lewis and Kellgren also caused palpable rigidity and deep tenderness of the lowest part of the abdominal wall, together with retraction of the testicle of the corresponding side in man, by injecting hypertonic saline solution into the first lumbar ligament. The significance of this experiment is lessened by the fact that the saline solution might have stimulated not only the somatic sensory, but also the relevant visceral-afferent nerves.

If now we turn to the clinical manifestations of the "viscero-motor reflex" several observations may be made. In the first place this protective mechanism does not always come into play. Secondly, it may be observed that the rigidity may either be generalized or strictly localized. The uterus, ovaries and Fallopian tubes are innervated by the first lumbar nerve. Unilateral salpingo-öophoritis is associated with muscle guarding of the lower abdomen limited to the same side, where as toxaemic accidental haemorrhage causes the most intense board-like rigidity of the whole abdomen, such as is seen in no other abdominal emergency. It is difficult to understand how a "commotion" in the first lumbar segment of the cord can determine which fibres of the abdominal musculature should contract to effect this varied and selective rigidity.

The most important observation of all is that, so far as I am aware, abdominal rigidity is nearly always, if not always associated with pain. It disappears under light anaesthesia, and is abolished by an injection of morphia. So far as is known light anaesthesia has no effect on the spinal cord. The action of morphia varies widely in different animals. In the dog and in man it depresses the pain apperception centre and stimulates the vomiting and salivary centres, but in therapeutic doses has no known effect on the spinal cord. The evidence with regard to the spinal cord is based on the response of somatic nerves, and the possibility cannot be excluded that morphia exerts a selective action, either on the visceral-afferent nerves themselves or on their synapses. The stream of impulses continues to reach the cord after the sensation of pain is abolished, and the rigidity should continue, unless it can be shown that both light anaesthesia and morphia do in fact exert a selective action either on the visceral-afferent nerves or on their synapses.

Kappis and Gerlach[31] report that the abdominal rigidity associated with visceral disease may be abolished by the paraverte-

bral injection of a local anaesthetic. I[20] have instanced a still more striking phenomenon. The woman suffering from toxaemic accidental haemorrhage of the concealed variety is very ill and in great pain. The uterus remains in tonic contraction, and the abdomen exhibits a board-like rigidity. The foetal parts cannot be felt, and the foetus is invariably dead. In such a case I infiltrated the ilio-hypogastric and ilio-inguinal nerves with a 2 per cent solution of novocain, using 10 c.cm. on either side. The result was astonishing. All pain disappeared and the abdomen became soft, so that the foetal parts could be felt with ease, and the patient was able to lie on her back in comfort. Not long afterwards she delivered herself of a stillborn child. The placenta followed almost immediately afterwards, together with a mass of old retro-placental blood. It is impossible to reconcile this event with Mackenzie's viscero-motor hypothesis, for anaesthetization of the skin of the lower abdomen could not[29] conceivably affect an area of commotion in the spinal cord which is occasioned by a stream of impulses from the uterus.

A cord reflex, such as the knee jerk, either occurs in repetitive form or it does not occur, and there is neither analogy nor warrant for the assumption that such a reflex can be selective and so varied as to cause muscle-guarding limited to one side of the lower abdomen in some cases, and generalized abdominal rigidity in others. Neither is the knee-jerk nor the plantar response abolished by an injection of morphia.

It is not easy to cause abdominal rigidity limited to one side by an act of the will, neither can abdominal rigidity be voluntarily maintained. It is therefore reasonable to maintain that it represents the activity of a reflex, and evidence that such a reflex exists is afforded by experiments performed on animals. The question at issue is whether it is, as is now generally accepted, a purely spinal reflex. It is possible that the reflex arc was in some manner broken by the paravertebral injections of Kappis and Gerlach. It might further be contended, although I think with considerable difficulty, that the subliminal impulses normally travelling in the relevant cutaneous sensory nerves are essential to the reflex.

It may therefore be concluded that abdominal rigidity rarely, if ever, occurs apart from pain, and is abolished by any procedure which abolishes the pain. This fact offers a strong argument in support of the view which I have advanced that the sensorium is involved in the "viscero-motor reflex." This argument does not, however, amount to proof because it is possible that morphia, ether, and other general anaesthetics may exert a specific action on the visceral-afferent nerves or on their synapses in the cord. It is, however, of interest to note that McSwiney and Downman[29] were impressed with the lack of correspondence between the general reflex activity of the hind limbs and the responses to visceral stimulation. They moreover found that transection of the spinal cord in the upper thoracic region markedly increased the motor responses to visceral stimulation in a decerebrate cat. This observation accords with, although it does not of necessity support the contention that central co-ordination is normally involved in the "viscero-motor reflex."

Summary.

1. Evidence is given which proves that the uterus, an abdominal viscus innervated by the sympathetic nervous system, is supplied by sensory nerves.

2. Uterine pain is a referred pain and there is no evidence of any deep, localized

uterine pain (the splanchnic pain of Ross). The quality of the pain is of the deep type.

3. Uterine pain is always referred to areas of skin supplied by branches of the 1st lumbar nerve, and can usually be abolished by anaesthetizing the cutaneous areas to which it is referred.

4. The pain arising from, or provoked in the uterus probably affords the most accurate delimitation of the 1st lumbar dermatome.

5. Uterine pain, in no way differing from that associated with dysmenorrhoea and labour, may be provoked in certain cases by applying a stick of silver nitrate to the cervical mucosa. It is probable that the endometrium is as, if not more sensitive than the cervical mucosa to this stimulus.

6. The most remarkable fact about this treatment with the silver stick is that it causes intolerable pain in some women and none in others. It is difficult to recall any other example in medicine where the same insult evokes such varied responses.

7. The cervix is not an inert structure, for the introduction of the silver stick frequently causes it to evince marked spasm. Pain is not usually experienced while the spasm lasts, but commences after the internal sphincter relaxes.

8. Tenderness to deep palpation over the tip of the transverse process of the 2nd lumbar vertebra, particularly on the left side, is almost invariably elicited in women who suffer from dysmenorrhoea. The dysmenorrhoea can often be "cured" for some months by one or more applications of the silver stick to the cervical mucosa.

9. Pain from the ovaries and fundus of the bladder is likewise referred to the lower abdomen, and to cutaneous areas supplied by the 1st lumbar nerve. The bladder pain is localized to the centre of the lower abdomen, while ovarian pain is usually limited to the side of the offending ovary. Chronic ovarian pain may frequently be cured by treating the cervical mucosa with the silver stick.

10. Evidence is adduced to suggest that the so-called "viscero-motor reflex" involves central co-ordination.

11. The observations and experiments which have been recorded are opposed to the hypothesis advanced by Lennander and modified by Morley.

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*Investigation of the Serum Protein Balance in Normal and Toxaemic Pregnant Women

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WE all know that whenever a pathological process takes place in the animal organism it will always interfere more or less markedly with the protein balance of the organism. Under normal conditions this balance remains at a strikingly constant level. Also pregnancy, which cannot be regarded as a pathological process but which nevertheless strains the female organism very considerably, brings about marked shifts in the protein balance. It is therefore easily understood that the balance is shifted still further, if the pregnancy is complicated by pathological processes.

Surgeons and physicians have fully realized the great therapeutic importance of keeping not only the protein balance, but also the water and salt balances of the organism within normal limits. But obstetricians seem but slowly to become aware of the special field within the pathology of pregnancy and parturition, where pronounced shifts occur in these 3 kinds of balance, and where further investigations might—as in surgery and internal medicine—be able to give fresh information on the origin of the disease and possibly lead the treatment on to new lines.

The disease consdered here is the so-called toxaemia of pregnancy, a term which dates back several hundreds of years, but which is actually irrational. It is true that all the signs and symptoms, or at least most of them, can be produced if the pregnant woman is exposed to poisoning with some substance or other; but, despite intensive search, we have not so far succeeded in demonstrating any poison in the organism of the pregnant woman which might give rise to the disease. A great many theories have been advanced in the course of time concerning the genesis and mode of action of this hypothetical substance, but the origin of the disease is to-day precisely as mysterious as it was in the days of Hippocrates. When we continue to use the term "toxaemia of pregnancy" it is because we have not got a more adequate expression at present for the disease in question. (See however Thygesen and Møller-Christensen.[1])

The paper here presented deals mainly

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with our investigation of the protein shifts in serum. As, however, the protein balance and the water balance are interdependent to a very great extent, it is impossible to keep these two things apart. We shall therefore refer also to some of the results we found concerning changes in the fluid balance in the hection where the results of the protein examinations are discussed.

Investigations.

The method of analysis applied by us for serum protein determinations and for fractioning of the proteins has been described by us elsewhere.[2] We therefore give no further account of it here, but refer the reader to Table I, which gives an idea of the accuracy of this method.

None of the results of analysis indicated in Table I occur in the remainder of our work, because for practical reasons the sodium sulphate solution used for fractioning of the proteins was weaker in these 10 control experiments than in the others. Thus the values found do not denote the actual amounts of albumin and globulin in the serum, for which reason the words albumin and globulin have been put in quotation marks.

Besides, by our own method all the sera have been examined by the method of total protein determination indicated by Bing.[3] The results are given for each individual case in the following tables.

The blood tests were in all cases made in the morning after 12 hours of absolute fasting. The blood was taken from a vein in the arm during the shortest possible stasis. Immediately after the coagulation of the blood the serum was separated by centrifuging and placed in a refrigerator until the analysis could be made.

Cases under Review.

The persons examined can be divided into 3 groups: I, normal non-pregnant women; II, normal pregnant women; III, toxaemic pregnant women.

The normal and the toxaemic pregnant women were patients of the Rigshospital, Copenhagen, and the normal non-pregnant women were pupils of the school of

Table I.

Total protein in serum, partly found, partly calculated as the sum of the found amounts of serum albumin and serum globulin.

Serum No.	"Albumin" found	"Globulin" found	Total protein		Difference	
			Calculated	Found	Absolute	%
	%	%	%	%	%	
1. Normal puerperium	6.25	1.10	7.35	7.30	0.05	0.7
2. Normal pregnant women ...	4.57	1.00	5.57	5.62	0.05	0.9
3. Toxaemic patient	5.51	1.32	6.83	6.72	0.11	1.6
4. Normal pregnant women ...	5.09	0.86	5.95	5.87	0.08	1.3
5. Normal pregnant women ...	5.56	0.83	6.39	6.44	0.05	0.8
6. Normal pregnant women ...	5.61	0.90	6.51	6.46	0.05	0.8
7. Normal non-pregnant women	5.85	1.09	6.94	6.97	0.03	0.4
8. Normal non-pregnant women	5.85	1.06	6.91	6.91	0.00	0.0
9. Toxaemic patient	4.12	0.75	4.87	4.98	0.11	2.2
10. Normal puerperium	5.60	1.77	7.37	7.37	0.00	0.0
Average	5.40	1.07	6.47	6.46	0.01	

midwifery. The latter were given the same food as the normal pregnant women in order to avoid differences in protein values due to different standards of living. The toxaemic pregnant women were living on the diet always prescribed in cases of toxaemia, that is a "sick" diet poor in salt, 1,000 ml. of fluid per day, and, of course, the necessary addition of vitamins. This sick diet is not poor in proteins, and an extra amount of protein was often added. The normal pregnant women were not kept in bed.

Group I.

Group I comprised 20 normal non-pregnant women between the ages of 24 and 35. The results of the analyses have been entered in Table II, from which it appears that the average value of total protein was 7.16 per cent, namely serum albumin 4.67 per cent and serum globulin 2.49 per cent. The mean of the albumin/globlin quotient was 1.94.

A comparison with Bing's method shows that the two methods give fairly conformable results, both as regards the average values and as regards the minima and maxima.

Group II.

Group II comprised 20 normal pregnant women in the 2 last months of pregnancy (3 in their 9th month and 17 in their 10th month). In none of these cases did the urine contain protein or pathological cellular elements of any kind. The systolic blood-pressure did not exceed 125 mm. Hg. and there was no oedema. No more than during pregnancy did these women present

Table II.

Serum protein, per cent in 20 normal non-pregnant women.

Serum No.	Total protein %	Albumin %	Globulin %	Per cent protein as Albumin	Per cent protein as Globulin	Alb./Glob. quotient	Total protein A.M. Bing.
1.	7.58	4.92	2.66	65	35	1.86	6.9
2.	7.21	4.72	2.49	65	35	1.86	6.5
3.	6.56	4.78	1.78	73	27	2.70	6.5
4.	7.34	4.56	2.78	62	38	1.63	6.3
5.	7.87	5.34	2.53	68	32	2.13	7.4
6.	7.51	4.72	2.79	63	37	1.70	6.5
7.	6.67	4.32	2.35	65	35	1.86	7.1
8.	7.21	4.22	2.99	59	41	1.44	7.0
9.	7.64	3.66	3.98	48	52	0.92	6.9
10.	7.20	4.30	2.90	60	40	1.50	6.9
11.	7.42	5.16	2.26	70	30	2.33	7.0
12.	6.96	4.44	2.52	64	36	1.78	7.0
13.	7.18	4.80	2.38	67	33	2.03	7.1
14.	7.23	5.08	2.15	70	30	2.33	7.7
15.	7.24	5.25	1.99	73	27	2.70	7.5
16.	7.19	4.22	2.97	59	41	1.44	7.4
17.	6.10	4.81	1.29	79	21	3.76	6.2
18.	6.11	4.36	1.75	71	29	2.45	7.2
19.	7.01	4.60	2.41	66	34	1.94	6.9
20.	7.80	5.02	2.78	64	36	1.81	7.0
Average	7.16	4.67	2.49	66	34	1.94	6.95
Minimum	6.10	3.66	1.29	48	21	0.92	6.2
Maximum	7.87	5.34	3.98	79	52	3.76	7.7

toxaemic signs and symptoms during parturition or the puerperium.

The results of the analyses appear in Table III, which indicates the following average values: total protein, 6.18 per cent; serum albumin, 3.75 per cent; serum globulin, 2.43 per cent; albumin/globulin quotient, 1.54.

While there was found a somewhat close accord between the results obtained by Bing's and our methods in the cases of non-pregnant women, there proved to be some difference as regards the normal pregnant women, in so far as the values were found to be 5 to 10 per cent lower when calculated by Bing's method than when calculated by ours.

A comparison between the average values of normal non-pregnant women and normal pregnant women (Table IV) shows the total protein value to lie 1 g. per 100 ml. lower in the latter than in the former cases, namely 6.18 and 7.16 per cent respectively. This reduction in total protein seems to be due exclusively to a decrease in the amount of serum albumin, which was 3.75 per cent in normal pregnant women and 4.67 per cent in non-pregnant women. The amount of globulin was practically the same in both groups (2.43 per cent in the former and 2.49 per cent in the latter).

TABLE III.

Serum protein, per cent, in 20 normal pregnant women.

Serum No.	Month of preg.	Total protein %	Albumin %	Globulin %	Per cent protein as Alb.	Per cent protein as Glob.	Alb./Glob. quotient	Total protein A.M. Bing %
1.	10	5.96	4.05	1.91	68	32	2.12	5.0
2.	10	6.28	3.82	2.46	61	39	1.55	5.9
3.	10	6.16	3.88	2.28	63	37	1.70	6.0
4.	10	7.04	4.14	2.90	59	41	1.43	5.7
5.	10	6.68	4.05	2.63	61	39	1.54	5.8
6.	10	5.65	3.43	2.22	61	39	1.54	5.7
7.	10	6.51	3.95	2.56	61	39	1.54	5.8
8.	10	6.23	3.71	2.52	60	40	1.50	5.5
9.	10	6.30	3.88	2.42	62	38	1.63	5.5
10.	9	6.31	3.88	2.43	62	38	1.63	5.5
11.	10	6.04	3.39	2.65	56	44	1.27	5.9
12.	10	6.41	3.60	2.81	56	44	1.27	6.5
13.	10	5.73	3.63	2.10	63	37	1.70	6.0
14.	10	6.10	3.66	2.44	60	40	1.50	5.9
15.	10	5.99	3.77	2.22	63	37	1.70	6.0
16.	9	5.82	3.77	2.05	65	35	1.86	5.7
17.	10	5.57	3.61	1.96	65	35	1.86	5.5
18.	10	6.01	3.49	2.52	58	42	1.38	5.6
19.	10	6.45	3.78	2.67	59	41	1.44	5.5
20.	9	6.26	3.55	2.71	57	43	1.33	5.8
Average		6.18	3.75	2.43	61	39	1.54	5.72
Minimum		5.57	3.39	1.91	56	32	1.27	5.0
Maximum		7.04	4.14	2.91	68	44	2.12	6.5

In other words the balance of the serum protein fractions proved to have shifted towards the globulins—the coarsely disperse phase of the proteins—a fact which manifested itself by a change in the albumin/globulin quotient amounting to 1.94 in the non-pregnant women and 1.54 in the normal pregnant women.

Expressed as percentages the shift means

a fall in the amount of albumin from 66 per cent in non-pregnant women to 61 per cent in normal pregnant women, and a rise in the amount of serum globulin from 34 per cent in the former to 39 per cent in the latter.

TABLE IV.

Average values of results of protein analyses in non-pregnant and normal pregnant women, in cases of mild and severe toxaemia, and in eclampsia patients.

	Serum protein analyses, a.m.				
	Bing	Th. and M.-C.			
	Total protein %	Total protein %	Albumin %	Globulin %	Alb./Glob. quotient
Non-pregnant women	7.0	7.16	4.67	2.49	1.94
Normal pregnant women ...	5.7	6.18	3.75	2.43	1.54
Mild toxaemia	5.3	5.95	3.26	2.69	1.21
Severe toxaemia	5.0	5.40	2.91	2.49	1.17
Mild and severe toxaemia ...	5.1	5.63	3.06	2.57	1.19
Eclampsia	5.1	5.56	3.27	2.29	1.43

GROUP III.

The third group comprised 24 toxaemic pregnant women, namely 10 cases without eclampsia and 5 cases with eclampsia.

The cases without eclampsia were again divided into 2 sub-groups: 8 mild cases of toxaemia and 11 severe cases.

Such a division, which is made on the basis of the clinical signs, presents numerous difficulties. First, it depends to a great extent on the observer's judgment; secondly, we cannot actually pronounce with full certainty on the degree of the complaint until after delivery and the puerperium; and finally we have experienced cases which were at first characterized as being of a mild or fairly mild degree, but which in the course of a short time (perhaps only a few hours) developed into severe toxicoses, sometimes even developing eclampsia.

Our division in mild and severe cases was based on the following facts.

Mild cases: No, or but moderately, visible oedema. Systolic blood-pressure not exceeding 150 to 160 mm. Hg. Albuminuria not over 3 or 4 per mille (Esbach) in 24 hours' urine. No, or but moderate, headache. Occasionally slight visual disturbances, but absolutely no retinal changes.

Severe cases: Generally pronounced oedema (face, hands and abdomen). Systolic blood-pressure exceeding 150 to 160 mm. Hg. Albuminuria generally over 3 or 4 per mille (Esbach) in 24 hours' urine, often a great deal more. Often severe headache. Often visual disturbances with retinal changes.

On this basis we divided, as mentioned above, the 19 cases of toxaemia without eclampsia into 8 mild and 11 severe cases.

In none of these cases (nor in any of those with eclampsia) was the pregnancy preceded by renal disease or hypertonia which might be thought to have been the cause of, or to have aggravated, the toxaemic condition.

The results of our investigations will appear from the following tables, where, besides the results of Bing's and our methods of analysis, we have added data which give an impression of the clinical

TABLE V.

Serum protein analyses of 8 patients suffering from mild toxaemia.

No.	Age	Para	Protein analysis made number of hours before parturition	Serum protein analyses, a.m.					Clinical signs and symptoms at time of protein analysis					Information on parturition			Course of previous pregnancies and parturitions
				Bing	Thygesen and Møller-Christensen												
				Total protein, %	Total protein, %	Albumin, %	Globulin, %	Alb./Glob. quotient	Blood-pressure mm. Hg.	Oedema	Albuminuria o/oo Esbach	Headache	Eye signs and symptoms	Course	Foetus	Placenta	
1	23	1	120	5.1	5.45	2.98	2.47	1.21	160/110	++	2.0	0	0	Forceps	Alive 3050 g. 50 cm.	1 White infarct	
2	32	3	72	5.8	6.35	3.92	2.43	1.63	125/75	+	0.5	0	0	Normal	Dead 950 g. 39 cm. mac.	0	1st and 2nd preg. and part. normal
3	23	3	72	5.7	6.36	2.92	3.44	0.85	125/75	0	1.5	0	0	Normal	Alive 2250 g. 43 cm.	2 White infarcts	1st and 2nd preg. and part. normal
4	41	6	24	5.6	7.03	3.96	3.07	1.29	155/100	0	0.4	+	Flickering ophthalm. nothing abnormal	Normal	Dead 2800 g. 50 cm. mac.	Abruptio placent. praemat.	4 first preg. and part. normal 5th part.: eclamp.
5	22	1	24	4.8	4.92	3.31	1.61	2.03	130/80	+	0.4	0	0	A: Norm. B: Norm.	Alive 2000/45 Alive 1850/45	0	
6	23	2	15	5.2	5.89	3.21	2.68	1.22	135/80	0	0.4	0	0	Normal	Alive 2900 g. 49 cm.	0	Eclampsia during 1st part.
7	17	1	68	5.1	6.09	3.19	2.90	1.10	145/65	+	1.4	0	0	Normal	Alive 2850 g. 48 cm.	0	
8	27	1	132	5.1	5.51	2.62	2.89	0.91	140/80	+	3.8	0	0	Normal	Dead 1400 g. 41 cm. mac.	Abruptio placent. premat.	
Average				5.3	5.95	3.26	2.69	1.21									
Minimum				4.8	4.92	2.62	1.61	0.85									
Maximum				5.8	7.03	3.96	3.44	2.03									

TABLE VI.

Serum protein analyses of 11 patients suffering from severe toxaemia.

No.	Age	Para	Protein analysis made number of hours before parturition.	Serum protein analysis a.m.					Clinical signs and symptoms at time of protein analysis					Information on parturition			Course of previous pregnancies and parturitions
				Bing	Thygesen and Møller-Christensen												
				Total protein, %	Total protein, %	Albumin, %	Globulin, %	Alb./Glob. quotient	Blood-pressure mm. Hg.	Oedema	Albuminuria o/oo Esbach	Headache	Eye signs and symptoms	Course	Foetus	Placenta	
1	25	2	27	4.6	5.15	2.55	2.60	1.00	165/100	++	4.0	+	Flickering ophthalm: o	Forceps	Alive 1800/44	8 white infarcts	Abortion (3rd month)
2	24	2	6	6.1	6.64	3.30	3.34	1.00	180/120	o	3.5	+	o	Induced partur. normal	Alive 2900/49	o	Eclampsia during 1st partur.
3	36	3	192	4.8	4.61	2.50	2.11	1.18	180/120	o	4.0	o	o	Normal	Dead 1900/46	Diffuse degenerative changes	1st and 2nd pregnancy and partur. normal
4	28	1	10	5.7	6.26	3.32	2.94	1.13	165/120	o	1.8	o	o	Forceps	Alive 2000/46	o	
5	27	2	72	4.5	4.97	2.86	2.11	1.35	150/95	+++	4.0	o	o	A. Forceps B. Extract.	Alive 3500/50 Alive 3600/50	o	Abortion (3rd month)
6	30	1	12	5.0	5.21	2.91	2.30	1.27	170/110	+++	3.0	+	Much flickering ophthalm: retin. oedema	Ind. part. A. Forceps version B. Extract.	Alive 2750/50 Alive 2650/50	o	
7	24	2	24	4.7	4.98	3.17	1.81	1.75	195/120	++++	1.5	+	Much flickering ophthalm: retin. oedema	Ind. part. A. Normal B. Extract.	Alive 3500/50 Alive 2800/50	o	1st pregnancy toxaemia
8	20	1	144	5.6	6.63	3.99	2.64	1.51	155/90	++	1.1	+	o	Induced partur. normal	Alive 2900/50	o	
9	36	1	19	4.9	5.37	2.87	2.50	1.14	180/100	++	7.5	+	o	Normal	Alive 2150/46	o	
10	35	2	9	4.1	4.31	1.76	2.35	0.75	170/80	++++	17.0	o	Flickering ophthalm: retin. oedema	Induced partur. normal	Alive 2950/50	2 white infarcts.	1st preg. and partur. normal
11	28	1	12	5.5	5.26	2.77	2.49	1.11	175/95	+++	16.0	o	Much flickering ophthalm: retin. oedema	Induced partur. forceps	Alive 3500/53	o	
Average				5.0	5.40	2.91	2.49	1.17									
Minimum				4.1	4.31	1.76	1.81	0.75									
Maximum				6.1	6.64	3.99	3.34	1.75									

state of the patient on the day the blood test was made. In addition the tables give information on each patient's age, parity, the course of labour and the condition of the placenta, and on the course of previous pregnancies and labours.

Table V illustrates the results of our examinations of 8 pregnant women suffering from a mild toxaemia. The average values as well as the maximum and minimum values have been entered at the foot of the table.

Table VI gives a corresponding survey of the results concerning the 11 cases of severe toxaemia.

A comparison between the average values from the 2 latter tables is seen in Table VII, lines 1 and 2.

Although we should, of course, be careful in drawing conclusions from such comparatively small numbers of cases, it is nevertheless a remarkable finding that the amount of total protein was smaller in the severe cases than in the mild ones, namely 5.40 and 5.95 per cent respectively. The fractioning shows that albumin and globulin contributed equally to the reduction, since the albumin/globulin quotient was practically the same in the 2 groups, that is, 1.17 in the severe cases and 1.21 in the mild cases.

The average values for all the 19 cases have been entered in Table VII, line 3. (It is, however, doubtful whether such a joining of mild and severe cases is at all justifiable; but that is a problem to which we hope to return on a later occasion). By comparing these values with those calculated for normal pregnant women (line 4) we found out that the patients suffering from toxaemia without eclampsia presented an unquestionable reduction in the total protein of the serum. This reduction seems to have been due exclusively to a decrease in the amount of albumin, since the amount of serum globulin had not decreased in these patients; on the contrary it had, if anything, increased.

The results of the examinations of the 5 eclamptic patients are shown in Table VIII. The eclampsia was mild in all 5 cases, each patient having had only one fit. In 4 cases the fit occurred before parturition and in 1 case after.

Of course we cannot draw any definite conclusions from this very small number of patients; but a comparison between the average values for eclamptic patients and

TABLE VII.

Average value of results of protein analyses in mild and severe cases of toxaemia, as well as for all cases of toxaemia collectively.

	Serum protein analyses, a.m.				
	Bing	Thygesen and Møller-Christensen			
	Total protein %	Total protein %	Albumin %	Globulin %	Alb./Glob. quotient
Mild toxaemia	5.3	5.95	3.26	2.69	1.21
Severe toxaemia	5.0	5.40	2.91	2.49	1.17
All cases of toxaemia without attendant eclampsia ...	5.1	5.63	3.06	2.57	1.19
Average values for normal pregnant women	5.7	6.18	3.75	2.43	1.54

TABLE VIII.

Serum protein analyses of 5 patients suffering from Eclampsia.

No.	Age	Para	Protein analysis made number of hours before parturition	Serum protein analysis, a.m.					Clinical signs and symptoms at time of protein analysis					Information on parturition			Cramps		Course of previous pregnancies and parturitions
				Bing	Thygesen and Møller-Christensen														
				Total protein, %	Total protein, %	Albumin, %	Globulin, %	Alb./Glob. quotient	Blood-pressure mm. Hg.	Oedema	Albuminuria o/oo Esbach	Headache	Eye signs and symptoms	Course	Foetus	Placenta	Number	Remarks	
1	28	1	2	5.3	5.31	3.59	1.72	2.03	150/100	0	1.0	0	0	Forceps	Alive 3900 g. 56 cm.	2 white infarcts	1	13 H. 25 M. A.P.	
2	21	1	21	5.5	6.03	3.63	2.40	1.51	170/100	++++	5.0	+	Flickering ophthalm: 0	Ind. part. forceps.	Alive 2550 g., 50 cm.	0	1	21 H. 50 M. A.P.	
3	24	1	12	5.3	5.73	3.30	2.43	1.36	160/95	0	22.0	+	Cons. dimn. of vis. ophthalm: not undertaken	Forceps	Alive 3200 g., 49 cm.	0	1	15 H. 30 M. A.P.	
4	17	1	22	5.1	5.91	2.98	2.93	1.02	160/100	+++	9.0	0	No subj. sympt. ophthalm: retin. oedema	Normal	Alive 2550 g., 47 cm.	0	1	1 H. 30 M. P.P.	
5	28	2	18	4.5	4.81	2.86	1.95	1.47	210/115	++++	15.0	+	No subj. sympt. ophthalm: retin. oedema	Ind. part. normal	Alive 1600 g., 48 cm.	0	1	8 days A.P.	Toxaemia in 1st pregnancy 1st partur. norm.
Average				5.1	5.56	3.27	2.29	1.43											
Minimum				4.5	4.81	2.86	1.72	1.02											
Maximum				5.5	6.03	3.63	2.93	2.03											

those for the other toxaemic patients suggests the following conclusions (compare Table IV, lines 5 and 6).

The amount of total serum protein proved to have become reduced to an equal extent in the toxaemic patients presenting eclampsia and those not presenting eclampsia. While the reduction was due exclusively to a decrease in the amount of serum albumin in the cases of the non-eclamptic patients, the eclamptic patients were found—compared with the normal pregnant women—to present a decrease both in serum albumin and in serum globulin.

For the sake of completeness we should mention the treatment to which our 5 eclamptic patients were submitted. Number 1 was given morphine and chloral hydrate according to Stroganoff's scheme. Number 2 was given morphine according to Stroganoff's scheme, 100 ml. of a 50 per cent glucose intravenously, 2 g. chloral hydrate 5 hours after the fit, and finally a total of 4 Percorten injections of 5 mg. each* in the course of the first 12 hours after the fit. Number 3 was given morphine and chloral hydrate according to Stroganoff's scheme. Number 4 was given Percorten only, 15 mg. in the course of 3 hours after the attack. Number 5, who was transferred to our department from a clinic in Copenhagen after she had had a typical eclamptic fit, was treated exclusively with Percorten (a total of 115 mg.). The patient was not given any morphine whatever, and she was delivered of a child in the normal way without narcosis a week after her admission after a medical induction of labour.

Finally, as regards Bing's test, it appeared that in the cases of the toxaemic pregnant women, as in those of the normal pregnant women, the values found were from 5 to 10 per cent lower than those obtained by our method (compare Table IV). The content of lipoid in the serum of pregnant women is probably the cause of the difference in the results.

* We thank the Ciba Farver & Farmaceutica Ltd., for having placed Percorten Ciba (desoxycorticosteronacetate) at our disposal.

Discussion.

In comparing our results with those published in previous papers we have found it expedient to treat each of the following groups separately: I. Normal non-pregnant women. II. Normal pregnant women. III. Pregnant women suffering from toxaemia without eclampsia. IV. Pregnant women suffering from toxaemia with eclampsia.

I. *Normal Non-pregnant Women.*

Table IX gives a survey of the average values which the various investigators indicate as normal for healthy non-pregnant women.

The last line of the table indicates our calculations of the average values for all authors collectively. We arrived at the following results. Total protein 7.30 per cent; serum albumin, 4.65 per cent; serum globulin, 2.65 per cent; albumin/globulin quotient, 1.75.

It appears from the table that the values accord fairly closely with each other. The differences found are due in the first instance to different methods of analysis. The investigators who used the gravimetric method (Siedentopf,[4] Albers[5]) and the refractometer method (Eufinger and Spiegler[6, 6a]) found the highest values, particularly as regards the serum albumin.

The results of the investigators who used Kjeldahl's method, or modifications of that method (Dienst,[7] Eastmann,[8] Adair,[9] Møller-Christensen and Thygesen[2]) do not differ very much from each other. Exceptions are Zangemeister[12] (Kjeldahl),

TABLE IX.

Comparison between the investigations made by the various writers of the serum proteins in normal non-pregnant women.

Writer, year, method of analysis, number of cases			Total protein %	Serum albumin %	Serum globulin %	Alb./Glob. quotient
Dienst (1918) Kjeldahl's method	9	cases	6.84	3.95	2.89	1.36
Zangemeister (1919) Kjeldahl's method	4	,,	7.78			
Plass and Matthew (1926) Wu's method	15	,,	7.11	4.42	2.69	1.64
Eufinger and Spiegler (1928) Refractom. method			8.4	5.5	2.9	1.90
Eastmann (1931) Hove's method	11	,,	7.1	4.5	2.6	1.73
Eastmann (1931) Wu's method	5	,,	6.8	4.5	2.3	1.96
Siedentopf (1938) Gravimetric method	18	,,	7.99	5.38	2.61	2.07
Albers (1939) Gravimetric method	10	,,	7.85	5.24	2.60	2.02
Neuweiler (1940) Henriques and Klausen's method	10	,,	6.35	3.69	2.75	1.34
Adair (1940)			6.5–8.2			
Møller-Christensen and Thygesen (1945) Bing's method	20	,,	6.95			
Møller-Christensen and Thygesen (1945) Thyg. and M.C.'s method	20	,,	7.16	4.67	2.49	1.94
Average values of the above results			7.30	4.65	2.65	1.75

who found high values, and Neuweiler[10] Henriques and Klausen's method), who found lower serum albumin values.

Investigations by Wu's colorimeter method[11] (Eastmann,[8] Plass and Matthew[12]) and by Bing's specific gravity method (Møller-Christensen and Thygesen) seem to have given results corresponding

TABLE X.

Comparison between the investigations made by the various writers of the serum proteins in normal pregnant women at the last stage of pregnancy.

Writer, year, method of analysis, number of cases			Total protein %	Serum albumin %	Serum globulin %	Alb./Glob. quotient
Dienst (1928) Kjeldahl's method	6	cases	5.97	4.05	1.92	2.11
Zangemeister (1919) Kjeldahl's method	4	,,	6.63			
Bergmann (1924) Refractom. method			6.7			
Plass and Matthew (1926) Wu's method	15	,,	6.59	4.07	2.52	1.62
Eufinger and Spiegler (1928) Refractom. method			6.76	2.33	4.34	0.60
Eastmann (1931) Hove's method	36	,,	6.3	3.9	2.4	1.6
Eastmann (1931) Wu's method	18	,,	6.1	4.0	2.1	1.9
Siedentopf (1938) Gravimetric method	36	,,	7.01	4.44	2.57	1.74
Albers (1939)	10	,,	6.95	4.42	2.44	1.80
Neuweiler (1940) Henriques and Klausen's method	24	,,	5.50	2.98	2.18	1.36
Adair (1940)			6.4			
Dexter and Weiss (1941)	10	,,	6.28	3.50	2.78	1.27
Dieckmann and Kramer (1941)			6.50	3.72	2.78	1.34
Møller-Christensen and Thygesen (1945) Bing's method	20	,,	5.7			
Møller-Christensen and Thygesen (1945) Thyg. and M.-C's method	20	,,	6.18	3.75	2.43	1.54
Average values of the above results (except those of Eufinger and Spiegler)			6.35	3.88	2.47	1.57

fairly closely to those obtained by Kjeldahl's method.

II. *Normal Pregnant Women (last stage of pregnancy.)*

It appears from Table X that, in the case of normal pregnant women, the various writers give proportional amounts of the different serum proteins which are fairly alike, with a single exception only.

latter half of pregnancy than in non-pregnant women. This reduction is due chiefly to a decrease in the amount of serum albumin (about 13 per cent), whereas the percental decrease in serum globulin is smaller (about 7 per cent).

The table shows Eufinger and Spiegler's results to differ a great deal from those arrived at by other writers. This is par-

TABLE XI.

Comparison between the investigations made by the various writers of the serum proteins in toxaemic pregnant women not presenting eclampsia.

Writer, year, method of analysis, number of cases				Total protein %	Serum albumin %	Serum globulin %	Alb./Glob. quotient
Dienst (1918) Kjeldahl's method		6	cases	4.63	3.31	1.32	2.51
Zangemeister (1919) Kjeldahl's method	Mild cases	26	,,	6.44			
	Severe cases	25	,,	6.04			
Bergmann (1924) Refractom. method				6.3			
Eufinger and Spiegler (1928) Refractom. method				6.44	1.62	4.82	0.34
Eastmann (1931) Hove's method	Severe cases	6	,,	5.4	3.1	2.3	1.3
(Siedentopf (1938) Gravimetric method (incl. eclampsia)		16	,,	6.13	3.54	2.59	1.40)
Albers (1939) Gravimetric method	Severe cases	8	,,	5.45	2.63	2.83	0.93
Neuweiler (1940) Henriques and Klausen's method		24	,,	5.15	2.56	2.59	0.99
Adair (1940)				6.0			
Dexter and Weiss (1941)	Severe cases			5.54	3.06	2.46	1.26
Dieckmann and Kramer (1941)	Severe cases			6.34	3.24	3.10	1.05
Møller-Christensen and Thygesen (1945) Bing's method	Mild cases	8	,,	5.3			
	Severe cases	11	,,	5.0			
Th. and M.-C's method	Mild cases	8	,,	5.95	3.26	2.69	1.21
	Severe cases	11	,,	5.40	2.91	2.49	1.17
Average values of the above results (Except those of Eufinger and Spiegler and Siedentopf)				5.64	3.01	2.63	1.14

The differences are also here due chiefly to the application of different methods of analysis. They may probably also be due to the fact that the patients were not all of them in the same month of pregnancy when the analyses were undertaken. Finally we cannot leave out of account the possibility that different social environments may have played a part.

Common to all the analyses is the fact that the total protein value is lower in the

ticularly the case with regard to the determinations of fractioning. For this reason Eufinger and Spiegler's results were not included in our calculation of the average values for all writers, which calculation presents the following percentages (compare the last line of the table).

Total protein, 6.35 per cent; serum albumin, 3.88 per cent; serum globulin, 2.47 per cent, albumin/globulin quotient 1.57.

III. *Toxaemic Pregnant Women Without Eclampsia.*

A survey of this group is given in Table XI. As Siedentopf's group of toxaemic patients comprises also cases with eclampsia we have bracketed his results, and his work is not included in the following review.

It is far more difficult to estimate these results than those reported for the non-pregnant women and for the normal pregnant women. The chief cause of the difficulty is the fact that the investigators do not agree with regard to the clinical estimate of the cases. While some writers regard a case as severe only when it is likely to develop eclampsia (in other words pre-eclampsia), others speak of severe cases only if oedema or hypertension or albuminuria or all 3 signs together are fairly well marked. In addition, it is often hardly possible to discover from the papers we have read how the writers estimated the degree of each case.

Moreover it is peculiar that most writers mention severe cases only. We should think that it might be of interest to know something of the protein balance in mild cases of toxaemia.

It appears from the table that Zangemeister and ourselves are the only investigators who have divided these patients into 2 sub-groups. Both Zangemeister and we arrived at the result that the total protein value is lower in the severe cases than in the mild ones. Besides, we believe to have shown that there is no difference between the 2 groups in the proportion of the protein fractions.

To obtain a general review of the results concerning the toxaemic pregnant women without eclampsia we have calculated the average values of all writers. Besides Siedentorpf's results we have also left out of account those arrived at by Eufinger and Spiegler, because the results found by the latter as regards the fractioning differ very much from those stated by other writers. The average values were then found to be as follows: Total protein, 5.64 per cent; serum albumin, 3.01 per cent; serum glo-

TABLE XII.

Comparison between the investigations made by the various writers of the serum proteins in toxaemic pregnant women not presenting eclampsia.

Writer, year, method of analysis, number of cases			Total protein %	Serum albumin %	Serum globulin %	Alb./Glob. quotient
Eufinger and Spiegler (1928) Refractom. method	Mild cases		6.75	3.63	3.12	1.16
	Severe cases		6.28	0.69	5.59	0.12
Eastman (1931) Hove's method	8	Cases	6.1	3.4	2.7	1.3
Wu's method	4	,,	6.2	3.7	2.5	1.5
Albers (1939) Gravimetric method	2	,,	4.81	2.10	2.71	0.77
Neuweiler (1940) Henriques and Klausen's method	3	,,	5.78	2.54	3.25	0.78
Adair (1940)			6.7			
Dexter and Weiss (1941)			5.10	2.60	2.59	1.00
Dieckmann and Kramer (1941)			6.70			
Møller-Christensen and Thygesen (1945) Bing's method	Mild cases	5 ,,	5.10			
Th. and M.-C's method	Mild cases	5 ,,	5.56	3.27	2.29	1.43
Average values of the above results (except those of Eufinger and Spiegler)			5.61	2.94	2.67	1.10

bulin, 2.63 per cent; and albumin/globulin quotient, 1.14.

IV. *Toxaemic Pregnant Women with Eclampsia.*

Table XII gives a survey of the protein investigations within this group of patients.

A direct comparison between the indicated results is extremely difficult, and it is perhaps a question whether such comparison is at all justifiable. First, each writer has examined only a small number of cases; secondly, a distinction is but rarely made between mild and severe cases; and thirdly, nothing is stated in the papers read by us as to the time at which the blood test was made. It is a point of great importance whether the blood test is made immediately after the 1st attack, or, for instance, after the 5th or 6th attack, or possibly before the first attack.

Be it stated at once that the results obtained in our 5 cases of mild eclampsia do not accord with those obtained by other writers. Compared with the cases of toxaemia without eclampsia we found a slight increase in the amount of albumin and a corresponding decrease in that of globulin. The other writers found that there is hardly any difference between the 2 groups of patients as regards the percentage values of the protein fractions.

The average protein values in eclamptic patients were as follows, according to Table XII (Eufinger and Spiegler's results having been excluded). Total protein, 5.61 per cent; serum albumin, 2.94 per cent; serum globulin, 2.67 per cent, albumin/globulin quotient, 1.10.

Commentary.

We shall now review the work here presented, and at the same time try to give an explanation of how the changes demonstrated in the serum protein balance of the normal and the toxaemic pregnant women have occurred.

As mentioned in the introduction, changes in the protein balance are nearly always accompanied by shifts in the water and salt balances. At any rate it is evident that the protein balance and the water balance are intimately connected. It therefore seems not only natural but also correct to study the two balances together (Thygesen and Møller-Christensen[1]).

The most certain criteria of changes in the water balance are obtained by determining the blood volume. For various reasons, however, we have not been able to do this. But, by determining the blood corpuscle-volume percentage (the haematocrit value) we may get, if not a definite, yet at least a tolerably good idea of the changes in the water content of the blood and thereby of the changes in the blood volume.

Table XIII is a summary in table form of all the investigations published in this paper. The figures not in brackets indicate the average protein values calculated from the results of the total number of investigations. The figures in brackets indicate the average values found by us. The bracketed figures in the last column of the table show the average values in haemocrit that we found within the 4 different groups.

The normal pregnant women presented a reduction in the total protein of about 13 per cent together with a decrease in the haematocrit value of a similar relative magnitude (from 39 to 34 volumes per cent), that is, the blood became more watery. The fractioning shows that the reduction was due chiefly to a decrease in the amount of serum albumin, whereas the decrease in the amount of serum globulin was smaller. Our calculations even show that the amount of serum globulin was practically the same in non-pregnant women and normal pregnant women, so that accordingly it was the

decrease in serum albumin alone that brought about the reduction in total protein.

Some investigations of the amount of blood in normal pregnant women have been published within recent years (Albers[5]). The various investigators all arrived at the result that an increase in the blood volume of between 10 and 20 per cent takes place within the last few months of pregnancy. Simultaneously the amount of albumin decreases in the same proportion, as appears from our investigations, whereas the amount of serum globulin is fairly unchanged.

We must conclude from these observations that the circulating amount of serum albumin is the same within the last few months of pregnancy as it is in the non-pregnant women, whereas the amount of circulating serum globulin is essentially greater in the pregnant woman than in the non-pregnant woman.

It appears further from Table XIII that the haemocrit value is the same in toxaemic patients without eclampsia as in the normal pregnant women, whereas the amount of total protein is decreased. The fractioning shows that this reduction is due exclusively to a decrease in the amount of serum albumin, probably owing to a loss of albumin through the kidneys. The amount of serum globulin is slightly greater if anything than that found in normal pregnant women.

As mentioned before, it is hardly correct to collect all cases of toxaemia without eclampsia in one group. Table IV shows that the severe cases presented lower values of both serum albumin and serum globulin than the mild cases. That the amount of serum albumin was smallest in the severe cases is easily explainable by the fact that these patients lost more albumin through the kidneys than those suffering from mild toxaemia. We shall return later to the causes of the low globulin values. The 2 groups also presented a difference, although, indeed, a small one, in haemocrit values, in so far as the haematocrit was 33 volumes per cent in the mild cases and 35 volumes per cent in the severe ones, that is, the latter group showed a tendency to haemoconcentration.

As regards the eclamptic patients our results do not accord with those of previous writers. We found a decrease in serum globulin and a corresponding increase in serum albumin, whereas others generally found an increase in serum globulin.

TABLE XIII.

	Total protein %	Serum albumin %	Serum globulin %	Alb./Glob. quotient	Haematocrit Vol. %
Normal non-pregnant women	7.30 (7.16)	4.65 (4.67)	2.65 (2.49)	1.75 (1.94)	(39)
Normal pregnant women (Final stage of pregnancy)	6.35 (6.18)	3.88 (3.75)	2.47 (2.43)	1.57 (1.54)	(34)
Toxaemia patients not presenting eclampsia ...	5.64 (5.63)	3.01 (3.06)	2.63 (2.57)	1.14 (1.19)	(34)
Toxaemia patients presenting eclampsia	5.61 (5.56)	2.94 (3.27)	2.67 (2.29)	1.10 (1.43)	(39)

It appears from the last column of Table XIII that the haematocrit value is the same in eclamptic patients and in non-pregnant women. This means that haemoconcentration has occurred and that the blood volume has become smaller in these patients than in normal pregnant women and in patients suffering from toxaemia without eclampsia, When this reduction in the blood volume is taken into consideration the conclusion is very naturally drawn that it is not only the amount of circulating albumin that is decreased in the cases of patients suffering from eclampsia, but that there occurs also a decrease in the amount of circulating serum globulin.

There are two possible explanations of the decrease in serum globulin. One is that globulin may be supposed to be lost through the kidneys or the endothelium of the capillaries. But if this should be the case the simultaneously occurring loss of albumin should be far greater than it actually is. The other, and in our opinion more likely explanation is that, if eclampsia is present, the power of the organism of producing serum globulin has somehow or other been diminished.

We believe that most investigators are inclined to think that the reduced amount of globulin is due to an impaired liver function. Attention should in our opinion be given also to the adrenal cortex. It is a well known fact that the hormones of the adrenal cortex are of great importance for the water balance, and very probably have a rather considerable influence on the production of serum globulin as well. The more one considers the problem of toxaemia of pregnancy the more often one meets with facts which seem to be traceable to the adrenal cortex. And, without wanting to prophesy, we would not be surprised if (in a short time) it became possible to find in the adrenal cortex the solution to the mystery of both toxaemia of pregnancy and eclampsia.

Conclusion.

(1) The following average values for serum protein have been found by a method of analysis developed by the authors.

(*a*) In normal non-pregnant women (20 cases): total protein, 7.16 per cent; serum albumin, 4.67 per cent; serum globulin, 2.49 per cent.

(*b*) In normal pregnant women within the 2 last months of pregnancy (20 cases): total protein, 6.18 per cent; serum albumin, 3.75 per cent; serum globulin, 2.43 per cent.

(*c*) In patients suffering from mild toxaemia without eclampsia (8 cases): total protein, 5.95 per cent; serum albumin, 3.26 per cent; serum globulin, 2.69 per cent.

(*d*) In patients suffering from severe toxaemia without eclampsia (11 cases): total protein, 5.40 per cent; serum albumin, 2.91 per cent; serum globulin, 2.49 per cent.

(*e*) In patients suffering from toxaemia with eclampsia (5 cases): total protein, 5.56 per cent; serum albumin, 3.27 per cent; serum globulin, 2.29 per cent.

(2) Taking into consideration the changes in the blood volume we concluded that in the cases with eclampsia the amount of serum globulin circulating in the blood seems to be reduced. Previously the general opinion was that the amount of serum globulin was increased.

(3) The causes of the changes in the protein balance are discussed, and attention is directed to the adrenal cortex, which probably plays a greater part in toxaemia of pregnancy and eclampsia than is generally supposed.

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Six Cases of Venous Intravasation following Intrauterine Lipiodol Injection

BY

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THE intrauterine injection of radio-opaque oils, such as lipiodol, is now such a common method of investigation of uterine abnormalities, and especially of tubal patency in cases of subfertility, that I have thought it of interest to put on record 6 cases of venous intravasation following this operation.

In Cases 1, 3, 4, 5 and 6 I carried out the investigation personally and these occurred after a series of some 200 to 300 cases of salpingography without mishap. Case 2 was operated on by a house officer at another hospital.

The conditions predisposing to this accident are said to be the following:

1. Injection of lipiodol before full post-menstrual regeneration of the uterine mucosa, that is, within a period of less than 8 days after the termination of menstruation;

2. Injection immediately after dilatation of the cervix;

3. Injection after curettage, before a proper interval has elapsed to allow of regeneration of the mucosa;

4. Injection just prior to the onset of menstruation, when the congested and oedematous mucosa readily allows of traumatisation;

5. Injection with excessive force.

Other predisposing factors are said, by Rohan Williams,[1] to be retrodisplacement or lateral displacement of the uterus with possible impinging of the oil-bearing cannula against the uterine wall. In my opinion this should not happen if a careful bimanual examination be done beforehand to determine the exact position of the fundus, if this be confirmed by the gentle passage of a uterine sound, and if the curve of the oilbearing cannula corresponds to that of the uterus. Examining the 6 re-reported cases we can see if and where the above rules were neglected.

CASE 1. Mrs. W. I carried out salpingography in December 1942, and both Fallopian tubes were found to be patent. Pregnancy followed almost immediately but unfortunately ended in miscarriage in the 3rd month, and the patient failed to conceive again. At her request salpingography was repeated in September 1945, when, owing to a misunderstanding, the operation was carried out just after the end of a monthly period (see contra-indication 1). Fig. 1 shows the right Fallopian tube to be freely patent, and the left possibly blocked at the cornua. There is intravasation of dye to the pelvic veins. The patient did not show any ill effect at the time although an X-ray of the lungs showed fine flecks of scattered lipiodol. After returning home, however, she experienced prolonged irregular vaginal loss, followed by a heavy "period," suggesting a mild pelvic inflammatory condition. Such a consequence was also reported by Flew[2] whose patient developed a left hemiplegia and a slight haemoptysis. Later, Mrs. W. became pregnant.

CASE 2. Mrs. B. The operation here was carried out by a house surgeon at an unfavourable time in the month, 4 to 5 days before the expected onset of the period. It is possible, also, that excessive pressure may have been used (contra-indications 4 and 5). The degree of intravasation of the pelvic veins is remarkable (Fig. 2). Haemoptysis or other ill effect did not follow. X-ray of the lungs was

not carried out for 2 or 3 weeks and, as will be seen later, a report of clear lung fields in this case at this date is not of great value.

Cases 3, 4 *and* 5. There next follow 3 cases which were all carried out within a week or two of each other, and which were the first examples of this complication that I had met. In all these cases the conditions for safety were fulfilled, and the only unusual common factor I was able to trace was a new and rather rough-surfaced rubber covering to the oilbearing cannula, this having presumably traumatized the cervix and permitted the ingress of lipiodol to the pelvic veins.

CASE 3. Mrs. F. Operation January 13th, 1944; last monthly period December 27th, 1943. The Fallopian tubes were patent to air and lipiodol was injected, intravasating the pelvic veins (Fig. 3).

The possible complications were not realized at the time and the patient was allowed to go home next day. She was re-admitted about a week later with a history of slight haemoptysis and soreness on the right side of the chest. X-ray of the chest taken on January 22nd, 1944, shows " a very fine, faint stippling giving a granular appearance through both lungs; ? lipiodol in minute quantities in the terminal capillaries." Slight haemoptysis continued for a few days without rise in pulse or temperature, and the patient was able to leave hospital within a week. X-ray of the chest taken on March 16th, 1946, reports " the lungs are now perfectly normal in appearance " (Fig. 7).

CASE 4. Mrs. C. Salpingogram, February 1st, 1944; last monthly period January 16th, 1944. X-ray report after injection of lipiodol—left Fallopian tube patent; right doubtful; intravasation of lipiodol to uterine venous plexus (Fig. 4). Three days later the patient had slight haemoptysis, and X-ray of the chest showed an appearance similar to Case 3 (Fig. 5). This case and the next were examined by a consulting physician who reported that no abnormal physical signs in the chest were present in either patient, but suggested that the X-ray appearances were due to minute pulmonary infarcts following a mild thrombophlebitis produced by some toxic principle in the lipiodol. X-ray of the chest repeated in this case on February 21st, 1944, showed excellent illumination without any trace of lipiodol (Fig. 6).

CASE 5. Mrs. S. Salpingogram, February 1st, 1944; last monthly period January 20th, 1944. X-ray shows intravasation of uterine venous plexus; both Fallopian tubes blocked at fimbrial ends. X-ray of chest as in Cases 3 and 4; haemoptysis 3 days later. End result good.

CASE 6. Salpingogram, July 24th, 1945; last monthly period July 10th, 1945. All conditions for safety appeared to be fulfilled in this case, but X-rays showed both tubes patent and venous intravasation to both iliac veins (Fig. 7). Subsequent history and X-ray findings as in previous cases.

Notes have been given of 6 patients in whom salpingography by means of the intrauterine injection of lipiodol was followed by pelvic venous intravasation. Sequelae have been noted and an attempt made to determine why these accidents took place.

COMMENTARY.

Robins and Shapiro, quoted by Rohan Williams[1] have reviewed a series of 1,000 salpingographies. Intravasation to the pelvic veins occurred in 18 cases without recognizable complications. Walther, quoted by Williams, on the other hand, reported pain in the chest, cough and blood-stained sputum as a manifestation of pulmonary oil-embolism, and 1 death from this complication. When this complication does occur, few if any consequences ensue, but some have been dangerous and some fatal.

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FIG. 1.

12.9.1945. Right tube freely patent; left tube ? blocked at cornua. Intravasation of dye.

A.B.

FIG. 2.

Lipiodol in all the pelvic veins, and extending up the ovarian veins out of the picture.

A.B.

FIG. 3.

Hysterogram. Large quantity of lipiodol present, and the appearance is very suggestive of intravasation to venous channels.

A.B.

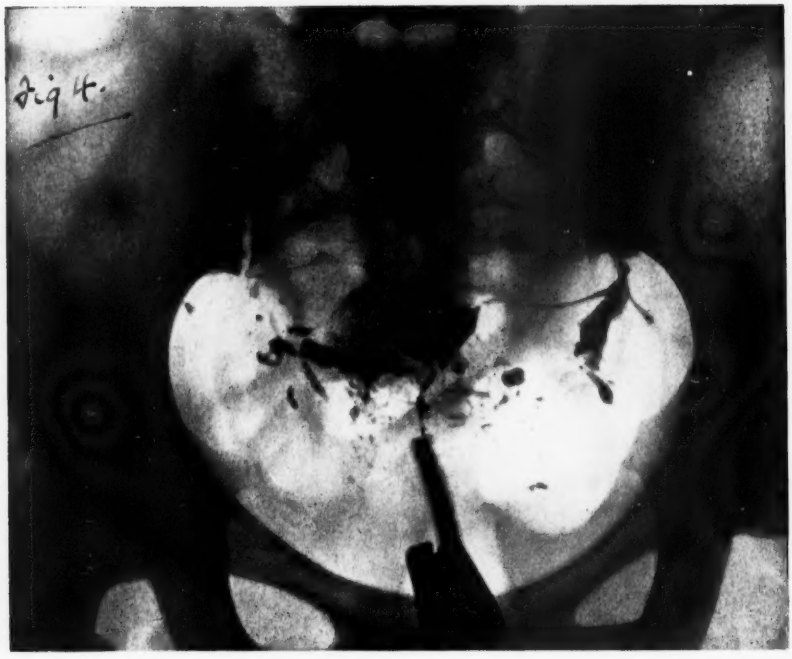

Fig. 4.

Left tube patent. Right tube doubtful. Some intravasation of oil to uterine venous plexus.

A.B.

FIG. 5.

Case 4. 14.2.1944. Appearances suggest minute pulmonary infarcts.
A.B.

FIG. 6.

Case 4. 21.2.1944. Shows excellent illumination without any trace of lipiodol.

A.B.

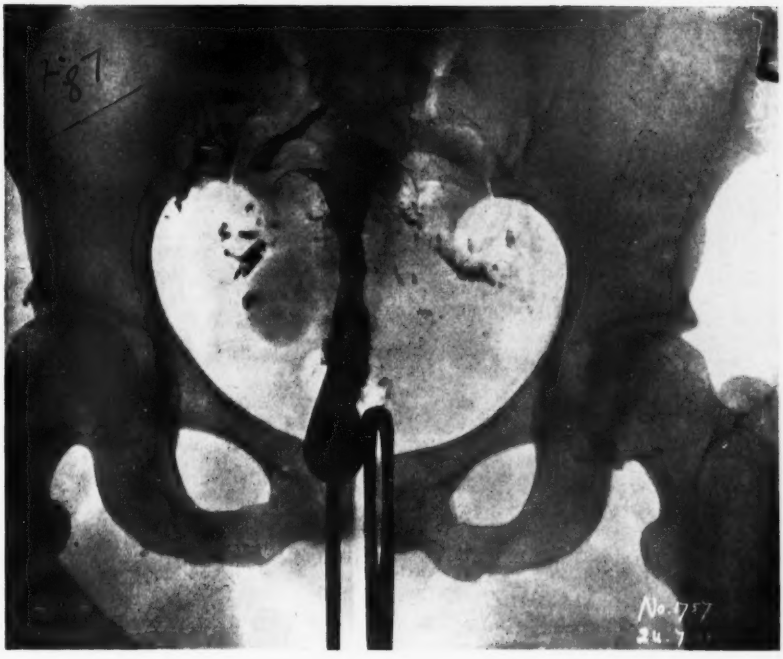

FIG. 7.

Lipiodol. X-ray. Both tubes patent. Both iliac veins contain lipiodol.

A.B.

Spinal Analgesia for Forceps Delivery in Abnormal Labour

BY

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I.

THERE can be no doubt that forceps delivery after prolonged labour, be the abnormality in the powers or in the passages or in both, may be a major operation, and as such demands an anaesthetic that will not be a contributory factor in the production of shock. Yet how often is this realized and skilled anaesthesia sought? I believe that so much attention has been paid to anaesthesia for Caesarean section on the one hand, and to the relief of labour pains on the other, that anaesthesia for forceps delivery has received far too little attention either in textbook or clinical teaching. The result of this neglect has been the administration of too many unskilled, prolonged, general anaesthetics in difficult deliveries. The anaesthetic itself is a factor to which, in the past, insufficient attention has been paid when death followed delivery; and, in the absence of severe haemorrhage or traumatic delivery, the (probably non-existent) condition of "obstetric shock" has often been diagnosed. Having seen such tragedies and many more near-tragedies, in which the maternal condition after delivery was worse than before, out of all proportion to the difficulty of the delivery, I am convinced that general inhalational anaesthesia (most usually nitrous oxide, oxygen and ether) must be responsible for many avoidable fatalities and much prolonged invalidism.

It may be claimed that this state of affairs calls only for more skilled anaesthetists, and to a certain extent this cannot be denied. At the same time it cannot be too strongly emphasized that anaesthesia for delivery, where two lives are at stake, is a special problem, and this fact is not always appreciated even by anaesthetists. The picture of a patient delivered under pudendal nerve block by a low forceps operation, even after prolonged labour, is in such contrast to the condition of those above referred to that it seems that a higher nerve block, such as is afforded by low spinal analgesia, must be the solution for difficult cases. Accordingly, a deliberate trial of spinal analgesia has been undertaken. The results were revealing and the fear that the anaesthetic would prove to be the last straw has been entirely banished. The description of cases in which spinal analgesia was used will, I hope, help to break down some of the prejudice against it, and also help towards the recognition, not only of its safety, but of its superiority to other anaesthetics for the mother, child and obstetrician. I have also included cases of eclampsia and the "failed forceps" case.

Caesarean sections were not included in this trial (although the prejudice against spinal analgesia is largely against its use in sections) as other factors are then involved; moreover the ideal anaesthetic for sections, local infiltration combined if necessary with pentothal, has few, if any, contra-indications. However, as most of the arguments in this controversial subject

involve Caesarean section, it must be referred to.

II.

An account of the opinions found in the more authoritative obstetric and anaesthetic textbooks is given here, as it illustrates the general confusion that surrounds this subject.

Beck,[1] for instance, mentions spinal analgesia only for labour pains and not for operative deliveries at all. Curtis,[2] operating in Cosgrove's unit, was forced to admit that the relaxation was all he could ask for, but states: "However, the danger of this method is ever present, and I very rarely use it." As a concession he describes a case in which it would be suitable ". . . that of prolonged second stage with a respiratory complication, provided the patient presents a completely dilated and effaced cervix." This sentence alone confirms his rare use of the method.

De Lee[3] held spinal anaesthesia to be very dangerous in obstetric practice, but admitted that the reasons were not all known. To quote his summing-up: "Anyway, why should we run any risks at all when we can do Caesarean sections just as well, and infinitely more safely, with local infiltration, and can do vaginal deliveries likewise under antesacral, or pudendal nerve block, or infiltration of the tissues." While I agree entirely in leaving out inhalation anaesthesia, I am partial to pudendal nerve block for low-cavity forceps operations, and believe that spinal block has a definite place in more difficult deliveries. Skill can be acquired in its use, and one must remember what Wevill has emphasized, namely, that the anaesthetist's task is not over once the drug has been injected into the theca; constant supervision is as necessary as with general anaesthetic.

Munro Kerr[4] states that spinal block is "most useful in cases of operative interference where a general anaesthetic is contraindicated." Here speaks experience, though it is hardly informative. Stander[5] condemns spinal analgesia for operative deliveries in general because of a number of unrecorded instances of death on the operating table during the performance of Caesarean section; but no information is offered as to the possible causes of these tragedies. Before this condemnation, however, it is stated that operations of any kind can be performed with the greatest ease.

From the anaesthetist's viewpoint, Minnitt and Gillies[6] devote only a dozen lines to anaesthesia for major obstetrical operations other than Caesarean section; but they do emphasize that the shock "of procedures such as prolonged forceps delivery . . . is considerable." While recommending various inhalational agents they apparently forget their earlier statement that "no general anaesthetic, however, can provide absolute protection against shock-producing stimuli in the same way that nerve block does, unless all tissues of the body are saturated by the drug to a degree approaching overdosage." They mention that "there is much evidence that pregnant women are particularly sensitive to spinal anaesthesia"; and, although they offer no explanation of this supposed sensitivity, they do indicate the obvious explanation when they state that "more tragedies could be avoided if it were realized that the operation of Caesarean section could usually be performed under an amount of anaesthetic which need be little greater than half the dose required for abdominal gynaecological operations." They might have added that with low spinal block, sufficient for vaginal deliveries, tragedies can all be avoided.

Wevill, in the book by Minnitt and Gillies, when discussing rachi-resistance,

mentions that "rachi-sensitivity is supposed to occur in certain toxaemias . . . and pregnancy," but that the theory of rachi-resistance "has not found general acceptance and it would certainly be most unwise to fall back on rachi-resistance to explain failures, without first of all scrutinizing most carefully the technique." Surely the time is long overdue when the same criticism should be applied to rachi-sensitivity and the above-mentioned particular sensitivity of pregnant women.

Langton Hewer[7] only refers to spinal block for deliveries by abdominal section, and states that "operative deliveries can be done under pure nitrous oxide-oxygen anaesthesia from the beginning. The addition of ether is rarely necessary." However, he states, too, that reflex shock can be minimized by deep general anaesthesia, and practically prevented by suitable nerve blocking.

Marshall,[8] in his monograph on lower segment Caesarean section, discusses fully the employment of ether, local and spinal analgesia. His case against ether is to my mind unanswerable: it increases atony, haemorrhage, acidosis, post-operative vomiting and ileus. Ether has, too, toxic effects on the liver and kidneys, lowers the peritoneal resistance to infection, and is a common cause of foetal asphyxia. Marshall quotes Schulcz as saying that "deaths after Caesarean section are either due to infection or anaesthesia," and believes this deserves a high place among obstetrical aphorisms. Of the advantages of spinal anaesthesia, Marshall mentions diminished haemorrhage and immediate closure of the uterine sinuses leading to a lower incidence of morbidity, absence of effect on metabolism, liver and kidneys, and a dynamic effect on the intestinal tract; consequently vomiting, atony and ileus are much less common in the puerperium. Finally the foetus is quite unaffected and is born as fresh as in a spontaneous birth. Much of what Marshall writes is applicable to vaginal deliveries in prolonged labour.

Under the heading "The peculiar susceptibility to spinal anaesthesia of women undergoing Caesarean section" Marshall examines the case against this agent. But as from this heading many controversial points arise, it will be studied more thoroughly in the discussion. The views of 3 experienced protagonists remain to be given—Maxson,[9] from the anaesthetist's viewpoint, Cosgrove[10] and Delmas[11] from the obstetrician's. Of spinal block in obstetrics, Maxson says that "it has never obtained recognition as a fully accepted method. Yet those who have used it intelligently are enthusiastic in its praise." He writes from personal experience of its use in Caesarean section; but for vaginal deliveries he falls back on Cosgrove's published views, because he has had "no experience in the field."

Cosgrove's experience is second to none in the use of spinal block for delivery, and his work should be studied by all who wish to try the method. It suffices here to say that he mentions all the advantages already listed by Marshall above, and adds those of absolute muscular relaxation, perfect analgesia, and the immediate post-operative ability to ingest food and fluid; also, less laceration due to greater relaxation, which itself leads to less morbidity and less shock. His account of the dangers included no mysterious unspecified factor peculiar to pregnancy.

Delmas concentrated on the condition of the cervix under spinal block and the opportunity afforded of manually dilating the cervix rapidly. Bittman[12] confirmed the use of Delmas's method in eclampsia "when rapid evacuation is called for," and he regarded the fall in blood-pressure as therapeutic. Modern obstetric practice is against rapid evacuation in eclampsia ex-

cept by section (itself a highly controversial procedure) and this has helped to put Delmas's views into a fog of disrepute. Summarizing trials of his method by other workers, Delmas complains of the general lack of understanding and of criticism without experience that still exists about spinal anaesthesia in obstetrics. His method is the digital dilatation of the cervix under spinal block " in cases in which failure to interfere was unjustifiable, and in which the artificial emptying of the uterus seemed to be necessary or at least desirable." He also stated that " clinical observations have shown that in spite of its effect in lowering blood-pressure, the procedure is quite safe." Delmas used it in only 4 per cent of his total deliveries.

Anaesthesia for difficult forceps operations emerges from this brief summary as the Cinderella of obstetric anaesthesia. In Caesarean section either one perfects one's own technique of local infiltration, or engages the help of an expert anaesthetist if the case is a serious one; while in simple low-forceps delivery a patient can stand up to a short inhalational anaesthesia if she has been in labour only for a normal time. Alternatively she can be delivered under pudendal nerve block if labour has been prolonged.

The value of the following series of cases does not lie of necessity in its numbers, but in the fact that they were all selected difficult cases, in which blood-pressure readings were taken throughout the duration of the operation. Further, in each case the spinal anaesthetic was given and the delivery conducted by the same individual—myself. As space would not allow a summary of every case with blood-pressure readings, Table I has been prepared, showing, it is hoped, as many as possible of the details that obstetricians would wish to know before they were satisfied that the alleged difficulties did really exist.

In 25 cases operative delivery was necessary through inability on the mother's part to deliver herself owing to malposition of the foetus, disproportion, inertia and to prolongation of labour, with various combinations of these factors. One case had no obstetric difficulty, but had collapsed under chloroform outside hospital just before delivery was attempted. Twenty-two were primigravidae, with an average age of 31 years, 11 being over 33 years of age. The average weight of the infants was just under 8 pounds, 16 being over 8 pounds. The most important indication, however, was the association of inertia and the resultant prolongation of labour. Seventeen of the 25 had primary inertia, 14 of sufficient degree to present the " full blown " picture with distension of bladder and colon—the most difficult type of obstetric case and one carrying a grave risk of postoperative shock.

The average duration of labour was just over 60 hours, in 7 cases being over 90 hours. This alone, I believe, should serve as a contra-indication to inhalational anaesthesia as commonly administered. Of the 14 cases of severe primary inertia, 3 infants died, 1 before delivery was undertaken, and 2 after—a mortality of 21 per cent compared with Bourne and Bell's 40 per cent, and in none of these could the anaesthetic be held responsible.

The duration in hospital for 23 patients, 2 being transferred to the City Fever Hospital on the 2nd day after delivery, was an average of 17.4 days.

Two mothers died; 1 from pulmonary embolus on the 17th day of the puerperium, and the second from streptococcal septicaemia contracted before admission. This case actually survived 9 days, probably because of the atraumatic delivery under spinal anaesthesia.

Tables II and III give details of 6 cases in which forceps delivery had failed outside

No.	Parity	Age	Main abnormality	Atony of bowel and bladder	Other abnormalities	Position of occiput	Hours in labour	Level of head in pelvic cavity
1	0	33	Primary inertia	+ + +	—	OA	59	Mid.
2	0	34	Secondary inertia	—	Malrotation	POP	65	Mid.
3	0	33	Primary inertia	+ +	Foetus dead	OP	142	Mid.
4	0	24	Secondary inertia	—	Malrotation	POP	66	Mid.
5	0	25	Disproportion	—	Dystrophia dystocia	OA	35	Mid.
6	0	28	Primary inertia	+ + +	—	OP	90	Mid.
7	0	29	Secondary inertia	—	—	OA	32	Low mid.
8	0	46	Primary inertia	—	Age	Lateral	40	Mid.
9	0	27	,, ,,	+ +	Disproportion	OP	47	Low mid.
10	0	24	,, ,,	—	Hypertension and disproportion	OP	(58)	High mid.
11				—	Hypertension and disproportion	Lateral	72	Mid.
12	0	37	,, ,,	+ +	Twins	OA / breech	96	Mid.
13	0	31	,, ,,	+	—	OP	100	Low mid.
14	0	37	,, ,,	+ +	$CHCL_3$ outside	Lateral	41	Mid.
15	1	36	,, ,,	+ + +	Disproportion and I.U.D.	Lateral	32	Mid.
16	0	29	,, ,,	+ + +	—	OA	44	Mid.
17	0	22	,, ,,	+ + +	Dystrophia dystocia	OP	60	Mid.
18	0	28	,, ,,	—	Contracted pelvis	Lateral	96	Mid.
19	0	30	,, ,,	+ + +	—	OA	32	Mid.
20	0	23		—	$CHCL_3$ outside " Collapse "	OA	27	Low mid.
21	0	34	Primary inertia	+	Disproportion and malrotation	POP	83	Mid.
22	1	30	,, ,,	—	Dystrophia dystocia	Lateral	18	Mid.
23	0	33	Secondary inertia	—	Foetus dead	OA	97	Low mid.
24	1	34	Disproportion	—	—.	Lateral	34	Mid.
25	0	39	Primary inertia	+	Toxaemia	Lateral	50	Mid.
26	0	38	,, ,,	+	—	Lateral	60	Mid.

TABLE I.

el of d in c cavity	Method of delivery	Weight of child lb.	oz.	Alive, stillborn or died	Pelvic infection	Morbid puerperium (M. of H. Standard)	Days in hospital	Dose of procaine in mg.	Blood-pressure before spinal, and lowest systolic level reached (mm. of Hg.)	Remarks
	Forceps	8	6½	A	–	–	17	120	140 to 100	
	Forceps, F. to P.	9	8	A	–	–	22	120	135 to 105	
	Perf. and Extr.	8	3	SB	+++	+	2	130	140 to 90	To fever hosp. Died 9th day of Group 'A' haemolytic streptococcal septicaemia
	Forceps, F. to P.	7	15	A	+	+	16	150	120 to 100	Died: Pulmonary embolism 16th day
	Forceps	7	2	A	+	+	16	150	110 to 60	Corrected by Trendelenburg position
	Man. rot. and forceps	10	4	A	–	–	13	150	120 to 60	No distress. Corrected spontaneously
mid.	Forceps	8	1	A	–	–	9	75	145 to 115	
	Man. rot. and forceps	8	2	A	–	–	13	100	165 to 100	
mid.	Spont. rot. and forceps	5	11	A	–	–	10	120	130 to 100	
n mid.	—		—	—	–	–	–	(i)130	190 to 70	Foetal head too high for delivery
	Man. rot. and forceps	8	7	D	–	–	24	(ii)100	130 to 100	N.N. death from Bact. coli. meningitis on 4th day
	2. Br. extract	6	8	A	–	+	21	100	120 to 60	Trendelenburg correction
	1. Forceps	7	2	A						Morbidity/mastitis
mid.	Man. rot. and forceps	6	14	A	+	–	16	50	130 to 110	
	Man. rot. and forceps	9	4	D	+	–	29	110	150 to 95	Foetal heart 170/min. Died of pneumonia
	Perf. and extr.	7	14	SB	+	+	42	120	120 to 70	Foetus died during labour
	Forceps.	7	14	A	+	–	16	80	130 to 105	
	Forceps	9	8	A	+	–	16	75	160 to 120	Rotation to OA, after 44 hours under N_2O, O_2, + ether
	Forceps rot.	5	11	A	+	+	33	100	165 to 150	Trial labour: Toxaemia at 36 weeks
	Forceps	8	12	A	–	–	10	100	180 to 130	
mid.	Forceps	8	10	A	–	–	16	80	140 to 110	Not collapsed on admission
	Forceps, F. to P.	10	9	A	+	–	13	100	130 to 75	
	Forceps	9	0	SB	–	–	14	120	124 to 80	Intracranial haemorrhage, SB
mid.	Forceps	10	15	SB	+++	+	2	75	145 to 128	To fever hospital. Recovered
	Forceps rot.	8	9	A	–	–	12	80	120 no change	Kielland's forceps no distress
	Forceps rot.	8	5	A	–	–	11	100	145 to 110	Kielland's forceps, no distress
	Forceps rot.	7	12	A	–	–	11	75	130 no change	Kielland's forceps, no distress

TABLE II

Cases admitted as "Failed f

No.	Parity	Age	Other abnormality	Bowel atony	Position of foetal head	Hours in labour	Method of delivery	Weight of child lb.	oz.	Alive, stillborn or died	Pelvic infection	Puerperal morbidity	Da hos
1	8	40	Multiparity	–	Lateral	20	Man. rot. forceps	12	2	SB	–	–	
2	0	36	Married 14 years	–	Lateral	18	,,	7	10	A	–	–	
3	0	43	Primary inertia	++	Lateral	46	,,	8	8	A	+	–	
4	0	32	—	–	Lateral	40	,,	7	12	A	+	–	
5	12	47	Multiparity	–	OA	28	Forceps	8	8	A	–	–	
6	8	34	Multiparity	–	Lateral	35	For. rot.	8	7	A	+	–	

TABLE III

Eclampsia.

No.	Parity	Age	Position of foetal head	Hours in labour	Method of of delivery	Weight of child (lb.	oz.)	Ali stillb or d
1	0	23	OA	?	Forceps	6	10	A
2	0	27	Lateral	24	Man. rot. and forceps	5	15	A
3	0	32	OA	20+	Forceps	7	1	A
4	0	34	OP	?	Man. rot. and forceps	6	12	A

ABLE II.

' Failed forceps outside."

eral lity	Days in hospital	Dose of procaine in mg.	Blood-pressure before spinal, and lowest systolic level reached (mm. of Hg.)	Reason for outside failure	Remarks
	9	120	150 to 90	Non-recognition of deep transverse arrest	SB through impaction of shoulders
	12	80	185 to 140	,, ,,	Forceps marks on face from outside attempt
	17	75	160 to 120	Cervix not fully dilated	—
	16	100	110 to 84	Non-recognition of deep transverse arrest	—
	10	120	110 to 55	Presenting part too high	No distress. Methedrine restored to 110/70 in 5 minutes
	11	100	140 to 120	Non-recognition of deep transverse arrest	—

BLE III.

clampsia.

ht ld oz.)	Alive, stillborn or died	Days in hospital	Dose of procaine in mg.	Blood-pressure before spinal, and lowest systolic level reached (mm. of Hg.)	Remarks
10	A	15	100	150 to 90	Slept during delivery
15	A	21	90	180 unchanged	Mastitis
1	A	18	80	150 to 130	——
12	A	12	90	165 to 110	Slept during delivery

hospital—another strong indication for avoiding further inhalational anaesthesia; and of 4 cases of eclampsia delivered under spinal block, none of the mothers and only 1 infant was lost.

The question of morbidity, having as it does a hard and fast definition, is also illustrated in Tables I and II in 2 different columns, the one showing morbidity by definition, and the other those cases which had a pelvic infection, irrespective of whether or not the temperature rose high enough to fulfil the definition. Unfortunately it is impossible to show a comparable series of cases delivered under general anaesthesia (as all my cases were specially chosen), but Bourne and Bell's morbidity-rate in inertia was 40 per cent. Of the 31 patients in Tables I and II, 14 developed a pelvic infection (45 per cent) but only 7 (22.5 per cent) were severe enough to be morbid. The 14 true inertia-syndrome patients, with an average of 66 hours in labour, included 7 (50 per cent) who developed pelvic infection, of whom only 3 (21 per cent) were morbid. Some of the credit for keeping this figure down must of necessity go to the sulphonamides, but many of the infections were due to anaerobic streptococci which do not respond to these drugs. In passing, it may be remarked that after spinal anaesthesia the ingestion of sulphonamide drugs is much more likely to be rapidly efficient than during the usual postoperative condition following inhalational anaesthesia.

Neither figures nor statistics can describe the well-being of women delivered under spinal block; their condition is entirely different to that commonly observed when prolonged labour is terminated under general anaesthesia. In many instances improvement is immediately manifested; in all cases, after a sleep for which every labouring woman yearns, they are fully able to take nourishment and regain strength rapidly, a factor of untold importance in keeping down the expectedly high morbidity.

Blood-pressure Changes.

Hewer disapproves of taking frequent blood-pressure readings, as he contends that it disturbs a conscious patient and might cause sore arms, but Maxson advises any beginner in spinal analgesia to take frequent readings "as the only means of learning the full effect of the dose given." Wevill regards such recordings as of little value and thinks they may distract the anaesthetist's attention from other signs of far greater importance. Maxson's advice was, however, faithfully followed by me not only as a means of becoming acquainted with the effects of different dosages, but also to add the great benefit of the reassurance thus provided. I did not come across sore arms; and as for disturbing consciousness, a woman in labour for a long period, even if she be highly strung and nervous, is in a state highly receptive to explanation of how her pain will cease. Many, contentedly finding the prophesy come true, drop off to sleep in spite of delivery and recordings of blood-pressure.

The guidance obtained by the records of blood-pressure was certainly of the greatest value, for a few patients had a fall in systolic level which in the presence of surgical shock or haemorrhage would have necessitated instant treatment, yet in none of these was there at any time signs of shock or distress. Further the pulse-pressure was always at least 20 mm. Hg.

At the end of the first 3 tables the initial blood-pressure and the level to which it fell is given, in order to correlate the dose and its effect on each patient. But in considering the fall in blood-pressure it must be remembered that this normally rises during labour, and that when the pain of uterine contraction is removed a certain degree of fall must be attributable to that alone, a fall

that must vary according to each patient's constitutional make-up and her threshold to pain. This is borne out by Hewer's observations on spinal block in patients with other causes of acute abdominal pain. In many cases, therefore, a mere recording of the actual fall in pressure may be totally misleading, that from 180 mm. to 100 mm. Hg. being of very different significance to a drop of 120 mm. to 40 mm. Both aspects of the pressure-drop are illustrated in Tables IV and V—the actual drop and the lowest systolic level reached in relation to the dosage of procaine used. It will be seen, in spite of misleading factors, that the larger the dose is the larger the drop—the site of injection being the same. This is, of course, well recognized; but it is not fully appreciated that women in labour do not show any peculiar deviation from this general rule, and that even in those patients in whom the systolic dropped to 60 mm. Hg. none showed any distress, respiratory, circulatory or mental.

As the trial proceeded, smaller doses were found to produce perfect conditions for delivery. Eventually (in some simple cases not here recorded) it was found that 50 mg. of procaine could be given by so slow an injection as to produce analgesia only of the perineum and vagina, and physical distress was caused by attempting the abdominal manipulation of the shoulder in rotating a posterior occiput—in such a case there would be no drop in blood-pressure beyond that due to removal of pain. The final dosage employed was 50–75 mg. of procaine for lower deliveries and 75–100 mg. for higher.

Table VI, showing details of 6 cases in which the blood-pressure was known before labour, illustrates the rise due to labour.

TABLE IV.

Average Drop of Blood-pressure in Millimetres of Hg., Correlated with Dose of Procaine.

Mg. procaine	Actual drops recorded (mm./Hg.)	Average drop (mm./Hg.)
150	20, 50, 60	43
130	50, 120	85
120	40, 30, 30, 50, 45, 60, 55	44
110	55	55
100	65, 30, 60, 15, 50, 55, 35, 20, 60, 26	42
90	0, 55	27
80	25, 30, 0, 45, 0	20
75	30, 40, 15, 0, 40	25
50	20	20

TABLE V.

Average Lowest Systolic Recording, Correlated with Dose of Procaine.

Mg. procaine	Lowest systolic level recorded (mm./Hg.)	Average (mm./Hg.)
150	100, 60, 60	73
130	90, 70	80
120	100, 105, 100, 70, 80, 90, 55	91
110	95	95
100	100, 100, 60, 150, 130, 75, 110, 84, 120, 90	105
90	180, 110	145
80	105, 110, 120, 140, 130	120
75	115, 120, 128, 130, 120	123
50	110	110

One patient was a known hypertensive and appears in Table I (No. 10): 2 spinal anaesthetics were given to this patient within 14 hours, for on the first occasion it was found that the presenting part was too high to attempt delivery.

TABLE VI.

Six Cases in which Antenatal Blood-pressure was known before Labour.

	Blood-pressure before labour	Immediately before delivery	Mg. procaine	Lowest blood-pressure recorded
1.	120/75	140/90	100	130/85
2.	120/80	125/95	100	105/60
3.	135/85	180/95	100	130/90
4.	130/80	165/110	100	150/100
5.	150/80	190/85	130	70/48
6.	130/85	165/95	100	100/80

In only 1 patient of the 36 detailed was the pulse-rate quicker after delivery than before, in most it was decidedly slower. The 1 case was due to severe bleeding from an episiotomy wound.

The size of the infant was found to have no influence on the ultimate lowest systolic pressure which, as has been already stated, fluctuated only according to the level of anaesthesia.

TECHNIQUE.

All injections were made into the 4th lumbar interspace. For the first few cases the lateral position was used, but it was soon found that the patient was better able to keep still in the sitting position, and, I believe, was more comfortable. As it undoubtedly made for an easier tapping, and better control of the level of anaesthesia, the sitting position was adopted early and was thereafter adhered to.

Full aseptic and antiseptic precautions and a virtual no-touch technique was used in inserting the needle. Iodine was preferred as a skin antiseptic and the proposed puncture-site wiped dry of iodine before an intradermal wheal was raised with 1 per cent procaine. A small-bore (22 gauge) spinal needle was inserted with the bevel turned to the side (so as to split the thecal coverings rather than tear them), and cerebrospinal fluid to the extent of 3 c.c. (about 55 drops) was collected into the ampoule of 150 mg. of procaine crystals, thus forming a 5 per cent solution. The solution was drawn into the syringe which was attached to the spinal needle, which was then turned so that the bevel pointed downwards before the necessary quantity was injected. The dose given was on the estimated difficulty of delivery. Barbotage was never practised.

Even in obese patients little difficulty should be experienced in tapping the theca, provided one has an eye for the midline and can palpate the iliac crests.

As procaine takes effect in 3 or 4 minutes and is fixed in 5, the patient was kept sitting for this period, and her pains had ceased by the time she had been arranged in the lithotomy position with one pillow under her head. Sleep was more probable when omnopon had been given just before delivery, but, as this tended to cloud the issue it was given only in the first few cases. The giving of ephedrine intramuscularly half-an-hour prior to operation was also abandoned when it was found to be irregular in its action, not preventing some of the greatest falls in blood-pressure. Instead, a close watch was kept for visible signs of collapse—pallor, cold clammy skin, and (most reliable of all according to Maxson)

a feeling of respiratory oppression. None of these signs was seen. By the time methedrine hydrochloride was reported on by Dodds, I had little need for its aid, though it was used in a few cases in which everything claimed for it was fully confirmed. As for side effects, only 3 patients vomited and not one complained of headache, in spite of the fact that no special instructions were given as to raising the foot of the bed, et cetera, after the return to the lying-in ward. Most patients naturally lay flat, sleeping, and were allowed to move as they liked when they awoke. No single cause apparently accounts for post-spinal tap headaches, but the majority of opinions favour the theory of leakage of cerebrospinal fluid leading to diminished intracranial pressure. Cosgrove's patients ceased to be troubled by headaches as soon as he used a small-bore needle. Lundy[13] believes the headaches to be attributable to disturbances of intracranial pressure and that "excessive attempts to puncture the dura and arachnoid, even without injection of a spinal anaesthetic agent, may result in headache, backache, and leucocytosis, but not usually in fever. These symptoms probably are attributable to meningeal irritation secondary to trauma and subarachnoid bleeding." Beattie and Dickson[14] mention small holes found in the theca. Short of careless technique leading to a true meningitis, I feel the single "tap", splitting the thecal fibres, with no more than a few seconds disturbance of cerebrospinal fluid pressure by using it as a solvent and replacing it, reduces the problem of headache to insignificance. Only one other possibility remains—some unexplained chemical irritation by the anaesthetic agent itself, and from this point of view procaine is generally regarded as the least toxic of all such agents. Burton,[15] in a recent series of cases complicated by cardiac disease and delivered under heavy nupercaine, was troubled by post-spinal anaesthetic headaches lasting up to a week. There is, however, in such cases, no need to use a heavy anaesthetic agent, for as good results can be obtained with procaine into the 4th interspace.

Discussion.

Although the results of any method are usually the best arguments "for and against" (and I hope it will be conceded that there is little fault to find with the results now presented), the subject of spinal analgesia for delivery is so controversial that a more detailed discussion is called for.

What is the nature of the usually undefined dangers of spinal analgesia for delivery? Cosgrove[16] mentions 3—vasomotor, circulatory, and respiratory paralysis, and to these must be added the possibility of some direct toxic action from absorption into the circulation of the anaesthetic agent. Rachi-sensitivity has already been commented on.

With analgesia reaching to the umbilicus, representing a spinal level of the 10th dorsal segment, the three dangers mentioned by Cosgrove are entirely avoidable. Too high an ascent of anaesthetic solution may, however, result "in lowering of blood-pressure to the point where the heart fails to get the needed nutrition" (Maxson) with resultant cerebral anoxia of the vital centres, and to progressive upward paralysis of respiratory mechanism—the intercostal muscles, the diaphragm and the medulla. But it is important to understand that this respiratory paralysis, with the exception of the intercostal paralysis, arises from cerebral anoxia through low blood-pressure, and not from direct action of anaesthetic solution. Blomfield[17] supports this view and states "that with novocain and allied drugs there is no fear of

paralysing the respiratory centre even if the injected dose travels up in the cerebro-spinal fluid. This does not apply to Stovain. Novocain is now being used fearlessly for operations above the umbilicus, indeed by some for operations in any part whatever."

Regarding vasomotor collapse, it cannot reasonably be held that blocking of only 5 sets of autonomic nerves (D.10 to L.2) will produce sufficient collapse to lead to a condition irreversible by the simple employment of the Trendelenburg position or the injection of methedrine.

Circulatory collapse, the third of Cosgrove's suggested dangers, is evidenced by fall in blood-pressure, and I believe, with the technique already described, that this fall is completely controllable and, if necessary, reversible. Maxson quotes Porter and Smith[18] as follows: "The criterion is not the absolute or percentile fall of blood-pressure *per se*, but whether there remains sufficient blood-pressure to carry on for a time at least the work of nerve cells in the brain and cord . . . the danger line may probably be placed at 60 mm. Hg." Maxson adds: "the young and robust will withstand a fall to 30 mm.; the aged and infirm are seriously embarrassed by a drop to 50 mm." Waldron[19] emphasizes that the important safeguard is the pulse pressure, and that as long as this stays above 20 mm. Hg. one should not be too much concerned about a pressure drop, "particularly if it is symptomless." Cosgrove stated that he had no cause to be concerned over excessive blood-pressure drop in a series of over 500 cases of all kinds; his patients had their blood-pressures recorded throughout, and he found an average systolic fall of 23 mm. Hg. for a 50 mg. dose and 38 mm. Hg. for a 75 mg. dose. Referring to these dosages, Maxson states that "low spinal anaesthesia is safe without exception" and, as Cosgrove, and Minnitt and Gillies point out, they are about half that which is usually used.

The disasters which have undoubtedly occurred are usually, as De Lee said, unrecorded and it is highly probable that the blood-pressure at the time was also unrecorded.

"The danger of spinal injection (Blomfield) is . . . if by any chance the dose used is excessive there is no means of extracting any part of it. In the course of many hundreds of injections there occurs, sooner or later, an unexpected collapse. This is probably to be attributed to the power which injected analgesics have of lowering blood-pressure." Minnitt and Gillies also include, under the acute circulatory failure known as neurogenic shock, the type of circulatory disturbance caused by factors which influence the nervous system directly, such as trauma or spinal analgesia. These opinions are quoted simply to emphasize that such disasters as have occurred have, in all probability, been due to overdosage, to poor observation of the patient's condition after the anaesthetic solution was injected, or to employment of drugs not so safe as procaine.

The final danger to be discussed is the possibility of toxic absorption of procaine from the spinal theca, and this is inextricably bound up with the question whether pregnancy carries with it some mysterious or, as Marshall puts it, "peculiar susceptibility." I believe that in Marshall's complete heading, "The peculiar susceptibility to spinal anaesthesia of women undergoing Caesarean section" lies the probable truth, for he offers four possible explanations, of which only one has anything to do with Caesarean section, and the rest refer to susceptibility arising from the state of pregnancy. Once more we find confusion —this time the confusion as to whether it is the pregnancy or the Caesarean section that is dangerous from the point of view

of spinal analgesia. I believe it is the latter, and that Marshall's words were well chosen, implying as they do that the susceptibility arises out of the mechanism of the operation. Many obstetricians and anaesthetists believe that there is something mysterious about pregnancy that makes spinal analgesia dangerous, but Macintosh and Mushin[20] state that "on commonsense grounds it appears to us to be a bogy to suggest that pregnancy makes a woman peculiarly susceptible to the effects of spinal analgesia." Hewer, however, writes that 'the mortality of Caesarean section under spinal block is for some reason high, and the method is not to be recommended." No more, no less, and we get no further forward.

Marshall suggests that there is a lowered capillary permeability in pregnancy favouring entry into the circulation of the anaesthetic agent. That this cannot have any real significance is proved by the fact that he eventually chose as the safest method local infiltration of the abdominal wall. Now 150 to 200 c.c. of ½ per cent procaine is commonly used for this method (and many operators are not afraid of greater quantities and higher concentrations); but this is a dose of 750 to 1,000 mg. injected into a much more vascular tissue than the enclosed space of the theca, where there are nerves with a recognized affinity for procaine, which "fixes" in 5 minutes. Moreover procaine may be given therapeutically intravenously (Lundy) in cases of cyclopropane epinephrine tachycardia.

Secondly, Marshall suggests that there may be some connection between the existing lipoidaemia and "increased toxicity of spinal anaesthesia during pregnancy." But he gives no clue as how the lipoidaemia is dangerous, even if it were admitted that there was a dangerous absorption of procaine from the theca, and I can find no warning in the literature against spinal analgesia in any other condition with increased lipoidaemia. Here again, local infiltration of large amounts as now widely practised would inevitably have led to innumerable disasters if there were any danger of this kind.

Thirdly, Marshall suggests an increased shift of blood volume into the splanchnic area and lower limbs leading to anoxia of vital centres. This is not peculiar to pregnancy as far as it is caused by vasomotor paralysis, and it is corrected simply by the Trendelenburg position. But if he includes the sudden release of pressure during the delivery of the child then, I think, he is getting at the root of the matter, for all anaesthetists are wary of spinal analgesia for any condition involving sudden lowering of intra-abdominal pressure, such as large retroperitoneal or ovarian cysts, and even in simple paracentesis for ascites it is traditional to prepare "brandy and a binder" in case of collapse. There is here a definite possible cause of collapse in Caesarean section, where there has already occurred the normal average blood-pressure drop due to the spinal block. If the collapse occurs before delivery it is much more likely to be due to overdosage and careless technique than to any mysterious susceptibility peculiar to pregnancy.

Marshall's fourth possible cause of such susceptibility is that labour pains and bearing-down efforts lead to more rapid diffusion of the anaesthetic agent in the spinal canal. De Lee also believed that during labour the fluid in the lower cord canal was "pressed up towards the medulla, causing respiratory paralysis." That this latter mechanism does not occur with procaine has already been pointed out, and I find it hard to believe that with 2 ml. (the maximum dose of an agent that is fixed in 5 minutes), the uterine pains and bearing down can be of any danger whatsoever,

quite apart from the fact that the level of analgesia reached was never noticed to be higher in patients who were still having strong pains. Few of my cases were having strong pains, and fewer still showed any uncontrollable bearing-down efforts.

To sum up this question, I feel that the conclusion is inescapable that the effect of spinal block with procaine depends on nothing more than the level of analgesia reached, and that the so-called "peculiar susceptibility of pregnant women" to spinal nerve block has no foundation in fact, beyond the possibility of collapse due to the comparatively rapid decrease of intra-abdominal pressure in Caesarean section. It is, as Minnitt and Gillies wisely remark, "the natural instinct of anyone, who has suffered the misery and ignominy of causing a death under an anaesthetic, to attribute it to some condition beyond human control." I cannot believe that it is beyond control, and Thomas's[21] series of Caesarean sections under heavy nupercaine is added proof that a technique, learnt with the aid of the sphygmomanometer, leads to smaller dosage and complete safety.

Surgical Shock.

Most writers now recognize the necessity of describing shock by an epithet indicating its cause. Before going further it must be stated that collapse due to spinal analgesia is not included as its aetiology is clear, and the essential difference, as Hewer says, is that there is no change in the volume of circulating blood. Maxson also remarks that slowing of the heart concurrent with lowering of blood-pressure constitutes an essential difference between the hypotension of spinal anaesthesia and that of shock. For the slower rate gives the heart muscle longer rest periods and, when accelerator impulses return, it is in good condition—quite the opposite from the vicious circle of surgical shock. Analgesia to the umbilical level has no effect on accelerator impulses, and in my cases the pulse-rate usually fell through removal of pain and substitution of rest.

How, then, may surgical shock arise during vaginal operative deliveries? Its initiation is probably determined by one or more of the following: (1) Haemorrhage from the uterus or lacerated tissues in the canal below; (2) plasma loss into traumatized pelvic tissues; (3) neurogenic factor, viz, repeated, powerful, sensory stimuli; (4) production and entry into the circulation of histamine-like substance as the result of trauma; (5) toxic effects of anaesthetic drugs; (6) psychogenic influences. I do not believe that "obstetric shock", in the shape of yet another mysterious factor peculiar to pregnant women, exists. All cases of shock following delivery are capable of explanation by one or more of the factors above mentioned and the term "obstetric shock," arising as it does from the desire to attribute disaster to some condition beyond human control should be rigorously excluded—it is, in fact, merely an "escape" diagnosis.

It will be agreed that the majority of my cases were strong candidates for secondary shock, yet not one suffered from it, and I submit that this is largely because the delivery was carried out under spinal block. It is generally conceded that haemorrhage from the uterus is less, and haemorrhage and plasma loss from tissue damage is also minimized because of the perfect relaxation of the passages obtained, an effect which also lessens the production of histamine-like substances. Reflex or neurogenic shock, from intra-pelvic manipulation, pulling and stretching, etc., is naturally completely prevented by nerve block.

Minnitt and Gillies depict a graph of the blood-pressure during a hernia operation under open ether in which the blood-pressure fell to 70 systolic and 65 diastolic following mobilization of the testis and handling of intestine. General anaesthesia cannot prevent this type of shock. Hewer states the modern view that there is a definite inhibition of the vasomotor centre by afferent nocioceptive stimuli, and that this type of shock can be minimized by *deep* (my italics) general anaesthesia, and practically prevented by suitable nerve blocking. "There has recently been a tendency to discount the effects of stimuli during light anaesthesia" and Hewer believes that the reaction has gone too far. I support Minnitt and Gillies in their view that deep anaesthesia can only inhibit such harmful stimuli by overdosage, and such overdosage itself leads to shock in the very attempt to prevent it. Nash epitomizes this aspect in stating that "very prolonged administration of a general anaesthetic can, and does, lead to the development of real surgical shock. The condition thus produced may be considered anaesthetic shock in the true sense and is quite distinct from the immediate and specific toxic effects of the drug. It is surgical shock whose chief predisposing cause is anaesthesia." Psychogenic shock may be looked on as a branch of neurogenic shock and, as I have already mentioned, I did not find any fear, even in nervous patients, provided time was taken to explain just what was going to happen.

It is contended, therefore, that, except for psychogenic shock, of which there is no more danger than in general anaesthesia, spinal analgesia is of supreme value in preventing surgical shock in difficult deliveries after prolonged labour. It is noteworthy that Bonney[22] always used spinal block to minimize shock in his Wertheim hysterectomies.

Operative Conditions.

The advantage of spinal block in ensuring complete relaxation is too well known to need repetition here, but certain other points should be mentioned: Firstly, with regard to dilatation of the cervix, I have no doubt that Delmas's practice of digital dilatation would be as easy as he asserts; for often I found, in spite of the primary vaginal examination suggesting full dilatation, that a centimetre or so of dilatation had yet to occur. In such cases the relaxation of the cervix enabled an easier and less traumatic completion of dilatation than under general anaesthesia. Occasionally manual rotation of the occiput was unexpectedly found to be necessary and distress was caused by abdominal pressure above the level of analgesia—a very small amount of pentothal remedied this. As uterine irritability is not affected the tendency that some patients have to form a contraction ring, as when the occiput is rotated, may dictate delivery face to pubes, as in Case 2. This was, however, the only time that this particular abnormality occurred. Several rotations were performed with Kielland's forceps applied by his method and only once was distress produced, and this during the application of the posterior blade as it reached the promontory of the sacrum. The dose in this case had been underestimated.

Occasionally the presenting part was low enough to deliver with episiotomy, and at this level spinal block has no great advantage over pudendal nerve block, provided the occiput does not need a difficult rotation; but when the presenting part was at mid-cavity level, or just above, in primigravidae, episiotomy was preferred to ironing out the vagina.

In grossly infected cases in which the operator envisages the use of sulphonamide powder on lacerated or incised tissues, spinal analgesia should be employed rather

than local or pudendal nerve block, for procaine inhibits the action of sulphonamides.

A further advantage of spinal block lies in the greatly diminished risk of vomiting and cyanosis, such as is not infrequently seen during the induction of inhalational anaesthesia at the end of prolonged labour —as a result the delivery is conducted in a quiet and peaceful atmosphere and postpartum aspiration pneumonia and pulmonary collapse are almost completely avoided.

The Third Stage.

Placental dystocia and haemorrhage from uterine atony was unknown in my cases, though in 5 the placenta was removed manually immediately after delivery as a deliberate policy. This practice arose out of the necessity, sometimes occurring after delivery under general anaesthesia, of having to give a second anaesthetic to remove a retained or partially adherent placenta, though latterly pentothal was used for this second anaesthetic. In spinal block deliveries immediate manual removal was given up, and pentothal was not required as the natural process always occurred.

Indications and Contra-indications.

Details of 3 types of case have already been given, but it is felt that attention should be paid particularly to the inertia syndrome (Goodall[23]) and dystrophia dystocia of De Lee, as indications *par excellence* for spinal analgesia. Williams's[24] description of the latter cannot be bettered: the distressing labour for days, exhaustion, the membranes long ruptured, signs of intrapartum infection and foetal distress, the cervix not fully dilated, the head high and the occiput probably lateral or posterior, "we are then dealing with one of the most serious types of case in obstetric practice." Goodall completes the picture of the depleted, infected mother, usually badly injured during instrumental delivery, with vomiting, dehydration, acidosis, intestinal and vesical obstinacy, use of the catheter, cystitis and sub-involution due to infection and inertia.

Three of the cases in Table I were judged to be true cases of dystrophia dystocia, while many others had more than half of the usual features. It was in such cases that De Lee considered Caesarean section would have been a better choice at the outset, and Williams agreed. Yet it is precisely in this type of case that one carries out expectant treatment the next time after consideration and decision upon vaginal delivery. I would only urge that obstetricians, thus having burnt their boats, will find all the advantages of spinal analgesia come to their aid when the moment for delivery arrives. Many of the terrors that follow prolonged deep general anaesthesia are in this manner banished. Goodall admitted, in drawing attention to the inertia syndrome, that he had nothing new to suggest in its treatment; it is a pity that the fact that general anaesthesia may well be the last straw is not more widely recognized. For cases which have already had inhalational anaesthesia for attempted delivery, or for early rotation of an occipito-posterior position, there can be little question that a second such anaesthetic should be avoided at all costs.

In eclampsia and non-convulsive toxaemia spinal block for delivery is equally beneficial, and Cosgrove here emphasized its use as there is no effect on the liver or kidneys, and by lowering the blood-pressure and slowing the heart the myocardium is relieved. There is no deleterious action on the respiratory tract, and the central nervous system is protected from noxious shock influences by complete blocking of peripheral neurons; further it does not cause cyanosis and has no deleterious effect on the child. Hewer regards

high blood-pressure as a contra-indication only if accompanied by marked arteriosclerosis, and he agrees that the method had been used with success in eclampsia.

In cardiac cases, Burton's series is sufficient indication of safety, though it is known that cardiac patients often escape difficult deliveries, and most can be delivered under local infiltration and pudendal nerve block.

I would go so far as to say that the only contra-indication—apart from skin sepsis and spinal deformity—is severe shock and hypotension, and that once these are corrected (as they should be prior to operative interference) spinal block will not only cause no further deterioration of the general condition but will help to prevent it.

The Child.

I do not think that any of the critics of spinal analgesia will deny the great advantage to the child. Sturrock points out that anoxaemia, due to over-dosage with analgesics or to development of cyanosis during general anaesthesia, is a preventable cause of foetal death, and that gas and oxygen "is much more difficult to administer successfully in pregnancy and labour than in general surgical cases if cyanosis is to be avoided." He also reminds us of Schreiber's pioneer work in tracing cerebral lesions in later life (spasticity, convulsions and mental retardation) to anoxaemia during delivery.

The benefit to the child is especially noticeable in prolonged labours and in trial labours. How often do we see a trial labour successful mechanically, the disproportion at the pelvic brim surmounted at the expense of the mother's strength, and the foetus still to be subjected to a mid-cavity forceps operation under general anaesthesia, an agent which may be the last straw to the child even more often than to the mother? Although spinal block relaxation cannot directly prevent either intracranial damage or foetal infection, it provides the easiest conditions for delivery, and by leaving the child free of any narcotic influences it is in better condition to ward off infection.

Finally, many obstetricians now agree that asphyxia from morphine is often really due to the superadded effect of a general anaesthetic, and, as Cosgrove points out, spinal analgesia obviates this well-recognized synergism. But, though well recognized, it is not sufficiently emphasized in current teaching, for the simple reason that general anaesthesia being customary it is easier to teach the traditional avoidance of morphine during the 4 hours before delivery, and to omit mention of the dangers of the combination of morphine and general anaesthesia.

Summary.

1. A series of deliveries under spinal analgesia in difficult obstetric cases is presented.

2. As a result of this experience and a search in the relevant literature, it is concluded that low spinal analgesia for difficult forceps delivery carries no danger peculiar to the pregnant woman, and that the disasters that have occurred are capable of a perfectly rational explanation and are not due to any mysterious susceptibility.

3. That as well as being a safe procedure it is maintained that spinal analgesia is of paramount importance in preventing secondary shock and minimizing haemorrhage and morbidity, and that it also prevents further deterioration in an already depleted patient.

4. Frequency of failure to recognize prolonged general anaesthesia as an important contributory factor in the production of shock is stressed, and an exhortation is

made to eschew the term "obstetric shock" as being an escape diagnosis.

5. The benefit to the child, particularly in prolonged and trial labours, is emphasized, especially as spinal analgesia avoids the combination of morphine narcosis with superimposed general inhalational anaesthesia.

I wish to express my gratitude to Professor R. W. Johnstone for permission to use patients under his care, and to Drs. E. Chalmers Fahmy and John Gillies for much encouragement and help. Also I wish to thank the many house surgeons who recorded the blood-pressures for me, and Sister Anderson of the Simpson Maternity Pavilion, who always had my "spinal packet" ready for instant use.

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Calcium and Phosphorus Metabolism in Pregnancy

(A Survey under War and Post-war Conditions)

FIRST COMMUNICATION ON THE CALCIFEROL FACTOR.

BY

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IN a previous communication[1] the general scope of this investigation has been outlined. The calcium intake and output figures for a group of control women and a group of women fed a supplement of calcium phosphate were given. The calcium and phosphorus balances were analysed. No correlation could be found in either of these 2 groups between the various factors usually considered to influence calcium metabolism, such as Ca : P ratio of the diet, protein or fat intake, potential acid-base balance of the food, et cetera. The figures, however, seemed to demonstrate that the probability of a positive calcium balance throughout pregnancy became greater above a certain level of calcium intake.

In the present communication, a further 14 cases* are dealt with, covering 67 48-hour balance periods at 6 weekly intervals from the 2nd or 3rd month of pregnancy to term. The calcium intake, output and balance figures for these further 14 cases are given in Table I. These figures, together with the figures given in the previous communication[1] are further discussed, splitting them into 3 groups in the following manner:

Group I. Controls, that is, no mineral or vitamin supplement, but on a self chosen diet with the optional addition of the statutory daily pint of milk. The figures for Cases 1 to 12 (controls throughout the period of observation) and the initial findings of Cases 13 to 22, before the supplementary feeding with calcium phosphate was started, have been given in the previous communication.[1]

In the present communication the figures given in the first part of Table I—from Cases 24 to 36 before supplementary calcium phosphate and vitamin D feeding was commenced—have also been treated as controls.

Group II. Cases on a self chosen diet, together with the following supplementary doses of calcium phosphate (the figures represent amounts of calcium and phosphorus elements per 24 hours).

	Calcium	Phosphorus
3rd to 5th months	0.64 g.	0.282 g.
6th to 8th months	0.95 g.	0.423 g.
8th month to term	1.26 g.	0.564 g.

Figures for Cases 13 to 22 were given in the previous communication,[1] and the figures for Case 23 are given, herewith, at the top of Table I.

Group III. Cases investigated in the same conditions as Group II cases, that is, on a self chosen diet with identical calcium phosphate supplements to Group II, and in addition a supplement of calciferol in the following doses.

* Case 23 (aged 26) had a normal previous pregnancy in April 1944. Cases 24 (aged 34), 25 (aged 29), 26 (aged 24), 28 (aged 33), 28 (aged 31), 29 (aged 33), 30 (aged 29), 31 (aged 35), 32 (aged 32), 33 (aged 34), 34 (aged 31), 35 (aged 25) were primiparae. Case 36 (aged 29) had one previous normal pregnancy in 1943.

3rd to 5th months	18,000 I.U. per 24 hours
6th and 7th months	27,000 I.U. ,, ,, ,,
8th month to term	36,000 I.U. ,, ,, ,,

The calciferol was administered in the form of pellets (Radiostol B.D.H.)—3,000 I.U. per pellet—and the women were instructed to chew the pellets like sweets, in order to ensure absorption.

The figures for Cases 24 to 36 are given in the second part of Table I.

those recommended as adequate by most authorities. Nevertheless (see Tables II and III), there were 42 per cent of negative calcium balances and 44 per cent of negative phosphorus balances in this group. A reduction in the Group III cases to 22.5 per cent negative calcium balances and 16 per cent phosphorus balance is too great to be accidental.

It is hoped that the data provided by the completed survey will throw light upon the following questions which are all of considerable practical importance:

1. The mechanism of action of calciferol.
2. What is the optimum dose of calciferol at different stages of pregnancy?
3. Are mineral supplements necessary, when the proper dose of calciferol is administered throughout pregnancy?

TABLE II.
Calcium Balances.

	Group I	Group II	Group III
Number of balances	68	36	44
Percentage negative balances	81	44	22.5
Percentage equilibrium	9	3	4·5
Percentage positive balances	10	53	73

Group I — Controls.
Group II — Calcium phosphate.
Group III — Calcium phosphate plus Calciferol.

(Balance figures under + or − 0.20 per 48 hours have been counted as "Equilibrium")

TABLE III.
Phosphorus Balances.

	Group I	Group II	Group III
Number of balances	68	36	44
Percentage negative balances	41	42	16
Percentage equilibrium	11	11	7
Percentage positive balances	48	47	77

COMPARISON OF CALCIUM AND PHOSPHORUS BALANCES.

The figures for all three Groups are shown in Tables II and III.

DISCUSSION OF THE CALCIFEROL (VITAMIN D_2) FACTOR.

The figures shown in Tables II and III provide almost conclusive evidence that calciferol has some influence on calcium, and to a greater extent on phosphorus metabolism.

Both calcium and phosphorus intake figures in Group II cases were higher than

MECHANISM OF ACTION OF CALCIFEROL.

In spite of the large amount of work done on animals, the exact mechanism of vitamin D action is still far from understood even in smaller laboratory animals. The action is

still more obscure in the more complex human organism. The most comprehensive monograph on the subject[2] emphasizes our ignorance. The authors of this monograph state: "Evidence is accumulating that the responses to vitamin D which have occupied most attention, that is, calcaemia, phosphataemia, modification of rates of absorption and excretion, ossification—are not primary changes, but are the signs of reactions to which they are secondary, and that back of all these there is a function of rendering calcium and phosphorus available to tissues, and a companion process of making the tissues more receptive to these ions—that is, stabilizing and integrating the relationship. How this is accomplished constitutes the major problem for investigation."

Shimotori, *et al.*[3] who studied the mechanism of vitamin D action in dogs by using radioactive phosphorus found increased urinary phosphorus excretion (found also in most of our Group III cases), and concluded nevertheless that calciferol probably does not exert its effect on phosphorus metabolism by improving intestinal absorption of phosphorus, but rather by intensification of the phosphorus turnover in bone with resulting hyperphosphataemia and decreased visceral phosphorus turnover. Though there was no increase in the plasma inorganic phosphorus figure in our Group III cases (in spite of the high daily dosage of calciferol), the marked increase in urinary phosphorus excretion in relation to faecal phosphorus excretion and the greater proportion of positive phosphorus balances, suggests an important influence on foetal bone growth. The postnatal follow-up findings of all groups, together with the findings on the succeeding groups of experimental subjects, to be published later—being given varying doses of calciferol without mineral supplements—should throw more light on this subject.

What is the Optimum Dose of Calciferol?

The doses specified above which were given to the Group III cases are much higher than those ordinarily given. They were decided upon as the result of previous experimental work in which the writer found difficulty in ensuring positive calcium and phosphorus balance throughout pregnancy on the usual doses.

A survey of the literature on this subject is not at all helpful. Park[4] states that pregnant women should be given 800 units of calciferol per day, but admits that he is not sure that this is the correct dosage. It is to be presumed that those who are responsible for the dosage in the daily Government capsule sold to mothers at antenatal clinics (which contains 800 units of vitamin D), shared Park's opinion.

In a more recent publication[5] McCune states that during pregnancy "an amount of vitamin D, equal to that contained in 5 teaspoonfuls of cod-liver oil, that is 1,700 units, may be required in addition to a high calcium intake to prevent a negative balance and guarantee calcium retention." Shohl[6] in his monograph on mineral metabolism writes "Four hundred units of vitamin D and 1 quart of milk daily should be included in the diet of pregnant women." No experimental authority for either of these statements is given.

On the other hand, Steck, *et al.*[7] proved that the tolerable limit of administration of the vitamin (without toxic symptoms) is 20,000 units per kg. per day for human and canine subjects. As the average weight of the women in Group III was 55 kg., it can be presumed that they would tolerate a dose of 1,100,000 units per day. The maximum dose given them at the end of pregnancy, that is, 36,000 units per day, allows a large margin of safety. None of these women complained of any unpleasant symptoms,

though it is doubtful whether such large doses are, in fact, necessary. In any case, the labour and postnatal details of the members of Group III do not bear out the suggestions made by such authors as Biehm,[8] who in a paper which provided singularly little experimental evidence, suggested that intermittent daily doses of 4,000 I.U. caused calcification of the placenta, and might cause calcification in the kidney of the new-born and premature calcification of the foetal head, or Finola, *et al.*[9] who claimed that on such minute doses as 250 units per day, there was radiological evidence of increased density of the foetal bones.

The findings in the next groups of women in this series should enable us to discover the optimum requirements for different phases of pregnancy with greater accuracy and also whether mineral supplements are necessary as well as calciferol, when adequate dietary intake of calcium and phosphorus is available.

Summary.

1. Calcium intake, output and balance figures are given on 14 further cases in the series—48-hour balance periods at 6-weekly intervals throughout pregnancy.

2. The calcium and phosphorus balances of all cases in the series considered up to date are analysed in three groups:

Group I. Control on self chosen diets.

Group II. On self chosen diets, together with a supplement of calcium phosphate.

Group III. As Group II, together with large doses of calciferol.

3. The table of calcium balances shows a marked decrease in negative balances in Group II as compared with Group III, and a still further decrease in Group III. Even in Group III, however, there were 22.5 per cent negative balances. The possibility that this may be due to an excessive dosage of calciferol is mooted.

4. The table of phosphorus balances shows no difference between Groups I and II with regard to percentage of negative balances—42 per cent. In Group III there is a reduction of the percentage of negative balances to 16 per cent.

5. The mechanism of action of calciferol is discussed.

6. Our ignorance as to the optimum dosage of calciferol during pregnancy is stressed and references given to the literature on the subject up to date.

Conclusion.

That positive calcium and phosphorus balances throughout pregnancy in normal women cannot be ensured by a high calcium and phosphorus intake alone. The addition of calciferol is essential.

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TABLE I.

Tabulation of Calcium Intake and Output Figures.

(The figures on each line represent the findings of a 48-hour balance period in terms of grammes of calcium element)

Date	Week of pregnancy	Case No.	Calcium intake					Calcium in blood	Calcium in urine	Calcium in faeces	Total calcium output	Calcium balance
			Milk	Cheese	Other foods	Sup.	Total					
6. 6.1945	20	23	2.75	Nil	0.32	1.45	4.52	9.8	0.58	3.96	4.54	−0.02
19. 7.1945	26		1.85	0.44	0.49	1.45	4.23	9.0	1.84	1.56	3.40	+0.83
14. 9.1945	34		2.01	Nil	0.41	2.08	4.50	9.6	0.59	3.34	3.93	+0.57
7. 3.1943	15	24	1.30	0.28	0.20	Nil	1.78	10.3	0.61	1.90	2.51	−0.73
13. 4.1943	21		1.41	0.19	0.35	Nil	1.95	10.8	0.63	2.10	2.73	−0.78
4. 4.1943	12	25	1.48	Nil	0.78	Nil	2.26	10.6	0.30	1.54	1.84	+0.42
18. 5.1943	19		1.03	Nil	0.52	Nil	1.55	10.3	0.67	1.96	2.63	−1.08
13. 7.1943	16	26	1.05	0.52	0.30	Nil	1.87	10.4	0.80	2.80	3.60	−1.73
25. 8.1943	22		1.23	0.76	0.19	Nil	2.18	10.2	0.79	1.57	2.36	−0.18
13. 7.1943	15	27	1.28	Nil	0.31	Nil	1.59	10.7	0.66	1.22	1.88	−0.29
25. 8.1943	21		1.72	0.22	0.53	Nil	2.47	10.5	0.42	0.38	0.80	+1.67
1.11.1943	12	28	1.02	Nil	0.44	Nil	1.46	10.1	0.74	1.29	2.03	−0.57
19. 2.1944	18	29	1.64	Nil	0.37	Nil	2.01	9.9	0.73	0.20	0.93	+1.07
1. 5.1944	9	30	0.86	Nil	0.47	Nil	1.33	11.0	0.79	1.16	1.95	−0.62
14. 3.1943	12	31	1.80	0.37	0.19	Nil	2.36	11.4	0.57	2.30	2.87	−0.51
20. 4.1943	17		1.40	0.37	0.30	Nil	2.07	10.8	1.10	6.10	7.20	−5.13
17. 4.1943	17	32	1.63	0.37	0.25	Nil	2.25	9.3	0.48	2.90	3.38	−1.13
31. 5.1943	24		1.45	0.08	0.40	Nil	1.93	9.3	0.75	1.98	2.73	−0.80
27. 7.1943	13	33	0.45	0.19	0.31	Nil	0.95	9.8	0.76	2.07	2.83	−1.88
10. 9.1943	19		0.97	0.34	0.61	Nil	1.92	10.1	0.89	1.29	2.18	−0.26
8. 1.1944	16	34	1.07	0.47	0.48	Nil	2.02	10.6	0.37	1.01	1.38	+0.64
19. 9.1944	13	35	1.82	Nil	0.41	Nil	2.23	9.0	0.59	2.56	3.15	−0.92
11.11.1944	14	36	1.00	Nil	0.45	Nil	1.45	10.0	0.46	0.99	1.45	Eq.
27. 5.1943	27	24	1.31	Nil	0.31	1.89	3.51	10.4	0.76	2.07	2.83	+0.68
9. 7.1943	33		1.48	Nil	0.30	2.52	4.30	10.2	0.84	1.83	2.67	+1.63
24. 6.1943	25	25	1.69	Nil	0.43	1.89	4.01	9.5	0.65	2.16	2.81	+1.20
6. 8.1943	31		2.04	0.49	0.47	Nil	3.00	10.0	0.70	1.36	2.06	+0.94
8. 9.1943	35		1.58	0.38	0.35	2.52	4.83	9.0	0.35	2.68	3.03	+1.80
6.10.1943	28	26	1.53	0.41	0.36	1.89	4.19	10.0	0.69	4.30	4.99	−0.80
17.11.1943	34		1.19	0.34	0.20	2.52	4.25	9.9	0.58	10.95	11.53	−7.28
23.12.1943	39		1.14	0.19	0.20	2.52	4.05	10.0	0.39	5.03	5.42	−1.37
6.10.1943	27	27	1.17	0.56	0.52	1.89	4.14	10.5	1.27	0.78	2.05	+2.09
14.11.1943	32		1.72	Nil	0.29	2.52	4.53	10.3	1.19	4.72	5.91	−1.38

TABLE I (*Continued*)

Date	Week of pregnancy	Case No.	Calcium intake					Calcium in blood	Calcium in urine	Calcium in faeces	Total calcium output	Calcium balance
			Milk	Cheese	Other foods	Sup.	Total					
6.12.1943	17	28	1.20	0.19	0.46	1.26	3.11	10.6	0.68	3.28	3.96	−0.85
10. 1.1944	22		1.35	Nil	0.49	1.26	3.10	10.6	0.68	1.70	2.38	+0.72
24. 2.1944	28		1.12	Nil	0.41	1.89	3.40	10.2	0.79	2.24	3.03	+0.37
3. 4.1944	33		1.30	0.19	0.48	2.52	4.49	9.8	0.79	3.90	4.69	−0.20
9. 5.1944	38		1.18	0.22	0.39	2.52	4.31	10.6	0.85	1.90	2.75	+1.56
4. 4.1944	24	29	1.42	Nil	0.40	1.26	3.08	9.8	0.48	0.74	2.22	+0.86
18. 5.1944	30		2.07	Nil	0.45	1.26	3.78	9.6	0.41	2.96	3.37	+0.41
25. 6.1944	35		2.02	Nil	0.40	1.89	4.31	11.2	0.33	2.16	2.49	+1.82
8. 6.1944	15	30	1.96	0.08	0.49	1.26	3.79	11.0	0.48	2.07	2.55	+1.24
4. 8.1944	25		1.45	Nil	0.50	1.26	3.21	10.7	0.77	1.20	1.97	+1.24
3.10.1944	31		1.48	Nil	0.45	1.89	3.82	10.0	0.81	2.29	3.10	+0.72
13.11.1944	35		1.72	Nil	0.62	1.89	4.23	11.2	0.78	2.32	3.10	+1.13
2. 6.1943	22	31	1.71	0.49	0.38	1.89	4.47	10.0	0.82	4.10	4.92	−0.45
21. 7.1943	29		1.46	0.49	0.31	1.89	4.15	9.6	1.09	1.81	2.90	+1.25
1. 9.1943	36		1.22	Nil	0.16	2.52	3.90	9.8	0.44	0.02	1.46	+2.44
10. 7.1943	30	32	1.55	0.12	0.27	1.89	3.83	9.7	0.89	2.60	3.49	+0.34
16. 8.1943	35		2.13	Nil	0.30	2.52	4.95	9.6	0.80	2.30	3.10	+1.85
22.10.1943	25	33	0.74	0.22	0.25	1.26	2.47	11.9	1.14	1.78	2.92	−0.45
6.12.1943	31		0.92	Nil	0.48	1.89	3.29	11.6	0.79	2.38	3.17	+0.12
18. 1.1944	36		1.15	0.41	0.52	1.89	3.97	—	0.56	2.12	2.68	+1.29
8. 2.1944	39		1.20	0.66	0.40	2.52	4.68	10.5	0.59	1.76	2.35	+2.33
22. 2.1944	22	34	0.97	0.65	0.45	1.26	3.33	10.8	0.76	2.44	3.20	+0.13
3. 4.1944	26		1.44	0.74	0.64	1.89	4.71	10.5	0.60	2.69	3.29	+1.42
15. 5.1944	32		1.53	0.51	0.65	1.89	4.58	10.2	0.68	3.64	4.32	+0.26
15. 6.1944	36		1.12	0.22	0.70	2.52	4.56	10.0	0.33	3.20	3.53	+1.03
9.11.1944	19	35	1.41	Nil	0.50	1.26	3.17	9.7	0.57	2.85	3.42	−0.25
12.12.1944	24		1.16	Nil	0.56	1.26	2.98	10.3	0.70	1.62	2.32	+0.66
24. 1.1944	30		1.40	Nil	0.39	1.26	2.85	10.3	0.56	1.95	2.51	+0.34
8. 3.1945	36		1.18	Nil	0.31	1.89	3.38	10.3	0.76	1.05	1.81	+1.57
16.12.1944	18	36	1.22	0.48	0.54	1.26	3.50	10.2	0.72	10.10	10.82	−7.32
25. 1.1945	23		1.32	Nil	0.48	1.26	3.06	10.0	0.50	2.09	2.59	+0.47
16. 3.1945	30		1.22	Nil	0.60	1.89	3.71	9.5	0.62	2.95	3.57	+0.14
3. 5.1945	36		1.20	Nil	0.50	1.89	3.59	9.0	0.46	3.63	4.09	−0.50
31. 5.1945	40		1.60	Nil	0.40	2.52	4.52	9.7	0.22	0.72	0.94	+3.58

Pulmonary Tuberculosis and Pregnancy

BY

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THE literature on this subject is bulky, and the views expressed widely divergent. In the main, 3 aspects of the problem are dealt with: (1) Is pregnancy a danger to a woman suffering from phthisis; does it tend to aggravate active disease or to reactivate quiescent disease in the lung? (2) To what extent may tuberculous women be permitted to bear children? (3) Is phthisis an indication for artificial interruption of pregnancy? This approach is inadequate, for it leaves out of consideration many important questions which arise in the management of these cases. However, even within this restricted field of study, much of the literature has served rather to obscure the problem than to illuminate it. The conclusions of the numerous workers are often contradictory, and this is not remarkable, for in many cases the basis on which these conclusions are founded is inadequate. Much of the literature, in short, is of no scientific value, for the material studied is incapable of supplying the answers to the questions posed. This has not deterred many writers from reaching emphatic conclusions and holding them with great tenacity. The confusing nature of much of the literature may explain, though it can hardly excuse, the remarkable neglect of this important problem in textbooks of general medicine. Even special textbooks on tuberculosis give very little space to the complication of pregnancy, which is adequately covered only in books on obstetrics. In the special literature, too, we find that many of the most exhaustive, objective and generally valuable studies of the subject have been made by obstetricians rather than by physicians. This is difficult to understand, for the combination of phthisis and pregnancy is frequent, and it calls for the exercise of the sort of judgment which physicians are apt to claim as their special province. Perhaps it is because they are unfamiliar with the speculative theorizing so prevalent in the literature of tuberculosis, that obstetricians have taken a more objective view of the problem. At all events, among the numerous papers on the subject a certain number are distinguished by a more scientific approach and these enable us to reach certain conclusions.

A traditional belief, existing from ancient times and expressed in the Hippocratic writings, credited pregnancy with a beneficial effect on phthisis, and this belief appears to have been general, both amongst the profession and the laity, until about 1850. During the latter half of the 19th century a number of writers expressed the view that pregnancy is harmful. This view replaced the earlier belief and gained increasing adherence until recent years, while many authorities drew the natural (though ill-substantiated) conclusion that if pregnancy be harmful to a tuberculous woman, artificial abortion must be the most satisfactory treatment. During the past 30 years the doctrinal pendulum has swung back and now occupies a more neutral position. The balance of opinion, however, still holds that pregnancy is harmful to the

tuberculous, although there is nowadays a healthy tendency to avoid sweeping generalization and to give each case individual consideration.

Literature.

In 1931, Robinson[1] published the results of a questionnaire addressed to a large number of different authorities, mostly in Britain, but including some in other countries. He reported that opinion was about 5 to 1 in favour of the view that pregnancy has a harmful effect upon phthisis, though many of these authorities gave little evidence in support of this view. This attitude was also evident in a discussion between physicians and obstetricians at the annual meeting of the British Medical Association in 1936.[2] A majority of our specialists in tuberculosis appear to regard pregnancy as a harmful "complication" in phthisis, and in active cases not a few of them advocate artificial abortion, provided the pregnancy has not advanced beyond 3 or 4 months. Some, indeed, seem to be more emphatic in their views than the available evidence warrants.

An attempt to analyse the general literature produces a feeling of confusion rather than enlightenment and only a few representative publications can be mentioned here. (Jameson[3] has written an admirable review of the literature.)

First, as to the alleged harmful effect of pregnancy on phthisis, perhaps the most frequently quoted writer is Rist,[4] who, in a study of more than 170 cases of pregnancy associated with phthisis, found that more than 80 per cent were worse after the pregnancy and more than 50 per cent were dead within 2 years of it. These figures are alarming, but they are open to 2 objections. Firstly, inadequate consideration is given to the nature, severity and extent of the tuberculous disease, and secondly there is no control material of cases of equal severity uncomplicated by pregnancy. Figures supporting the same view have been published by many authors, including Sergent and Moricard,[5] Trembley,[6] Hutchinson,[7] Bernard,[8] and Norris and Murphy.[9] It is noteworthy that those writers who produce the most alarming figures are nearly all open to the same criticism as Rist. In papers including a control study, though in a number of cases an unfavourable effect of pregnancy is claimed, its degree is seen to be very much less than that asserted by Rist. One of the best studies of this type was published in 1925 by Forssner of Stockholm.[10] He found that in the less advanced cases of phthisis there was very little difference in the after histories of those women who had undergone pregnancy, as compared with those of a control series. In the more advanced cases of phthisis, however, there appeared to be a somewhat less favourable outcome in the women who had undergone pregnancy, though its degree was less than had been described by other writers. Forssner's results are summarized in Table I, taken from his paper.

A paper by Cohen[11] analyses the results in 100 tuberculous women who underwent pregnancy and labour, with the conclusion that "pregnancy and labour *per se* rarely exert any harmful effect on the progress of pulmonary tuberculosis."

A number of other writers have made comparative studies of the after histories of tuberculous patients, some undergoing pregnancy and some not, and have reached the conclusion that no significant difference can be shown between them. Among these are: Barnes and Barnes,[12] Hill,[13] Brindeau *et al*,[14] Glaser,[15] and Schultze-Rhonhof and Hansen.[16] To sum up, the bulk of the evidence indicates that in minimal or quiescent cases of phthisis pregnancy exerts no harmful effect, but in cases of more active disease pregnancy may be harmful in a proportion of cases, though it is certain that

this harmful effect has been much exaggerated by many writers.

Influence of Pregnancy on Phthisis.

In what way may pregnancy exert a harmful effect on phthisis? Many theories have been advanced, some of them rather academic. Chemical factors, e.g. depletion of calcium or rise in cholesterol content of the blood, have been invoked, though the latter has been held to be protective rather than harmful. Some authors, e.g. Bar,[17] have pointed to the decline in tuberculin sensitivity which is observed in some cases of phthisis during pregnancy and have claimed that these are the cases in whom danger of aggravation of the lung disease exists. Bar went so far as to advocate therapeutic abortion in cases in whom the tuberculin reaction is absent or feeble, though it would seem that it might be the severity of the lung disease rather than the fact of pregnancy which is responsible for the relative "anergy." Most stress has been laid on mechanical factors: the enlargement of the uterus and the consequent progressive rise of the diaphragm during pregnancy. The increasing restriction of movement of the diaphragm was formerly held to be the harmful factor, but more recently this theory was seen to be in conflict with the theory of collapse therapy and it has accordingly been modified. It is now held that the elevation of the diaphragm during pregnancy is a favourable factor, but that the sudden descent during labour is harmful. This is held to explain improvement of the lung disease during pregnancy, which is sometimes observed, followed by rapid deterioration after delivery. It is true that some cases of phthisis undergo exacerbation during or shortly after the puerperium. The observation of a case of this type is sometimes responsible for emphatic views on the danger of pregnancy

Table I.

Comparison of after-history of women suffering from phthisis during a two-year period after pregnancy with that of similar patients in whom there was no gestation which could have influenced the development of the disease (after Forssiner).

Observation period	Stage (Turban)		Aggravated Per cent	Dead Per cent
One year: (Pregnant: 203 cases) (Non-pregnant: 396 cases)	I	Pregnant	28	1
		Non-pregnant	23	2
	II	Pregnant	33	6
		Non-pregnant	21	6
	III	Pregnant	19	46
		Non-pregnant	20	37
Two years: (Pregnant: 185 cases) (Non-pregnant 359 cases)	I	Pregnant	28	12
		Non-pregnant	27	14
	II	Pregnant	35	17
		Non-pregnant	30	14
	III	Pregnant	4	70
		Non-pregnant	10	63

to the tuberculous, though a more general view of the evidence might produce less extreme views. A factor of great importance which has been ignored by many writers is the influence of social and environmental conditions. It is hardly necessary to invoke highly theoretical conceptions of biochemical, endocrine, or even mechanical changes to explain a deterioration in the lung disease of a recently delivered woman when we consider the drastic changes in her life which the advent of an infant brings. The strain of lactation, the physical exertion of caring for a baby and washing its clothing, disturbed sleep, the added difficulties of housework, shopping and caring for the rest of the family, to say nothing of the financial burden represented by the new child, seem more than enough to account for an exacerbation of the lung disease. All these adverse factors apply in inverse proportion to the family income. In this, as in all other aspects of tuberculosis, the social factor is important, but it is often little heeded in academic controversy. It may well be that the widely different conclusions reached by different authors as to the effects of pregnancy on phthisis are largely due to neglect of the social factor, which can vitiate the most carefully chosen cases.

Therapeutic Abortion in Phthisis.

This subject appears to provoke as much heated polemic as any other in the whole field of medicine, but a brief study of the available evidence leaves little doubt as to the correct attitude. As concluded above, a certain number of cases of phthisis deteriorate after pregnancy, though this proportion is not large and may well be explained largely by social factors. However, the possibility of exacerbation of the lung disease is regarded by many as adequate grounds for advocating abortion as a method of treatment. If this is to have any scientific justification, evidence must be sought showing that in general the harmful effects are avoided if the pregnancy be interrupted. A study of the literature will soon convince any impartial person that no such evidence exists. There are relatively few studies in which an adequate series of tuberculous women in whom pregnancy has been artificially interrupted is compared with a series of cases of equal severity undergoing full time pregnancy and labour. Such studies as do exist have failed to show that an artificially interrupted pregnancy has in general any less unfavourable effect on the course of the lung disease than a full time pregnancy. Some few authors, for example, Czazkes[18] have claimed a more favourable outcome in aborted cases. Pissavy and Lejard,[19] in a criticism of Czazkes' paper, have pointed out that his conclusions were open to question, since he does not give details of the severity of the cases considered, and that even if the most favourable possible interpretation were accepted it would mean that to secure a $3\frac{1}{2}$-year survival in 17 women it would be necessary to sacrifice 100 pregnancies. This means the certainty of unnecessarily sacrificing about 80 infants, and since it is impossible to decide in any particular case whether the outcome will be favourable or otherwise it is not easy to justify sacrifice of the infant. Barnes and Barnes[12] found that the outcome in a series of women in whom pregnancy had been artificially interrupted was less favourable than in those in whom it had proceeded to term, and this result has also been obtained by a number of other workers.

Even those who advocate therapeutic abortion are agreed that it must be completed within 3 to 4 months of conception. Since relatively few cases come under observation so early, and since the benefit

in any particular case is problematical, we must conclude that abortion is justified only in a small number of cases where special circumstances exist. It can play little part in the solution of the difficult problems which arise in the treatment of pregnant tuberculous women.

As regards the child, it is clear from many studies that the infant of a tuberculous mother has almost as good a chance of being normal at birth as that of a healthy woman. Congenital tuberculosis is extremely rare, and provided the child can be protected from the risk of infection by its mother after birth its chances of survival and normal development are very good.

The Extent of the Problem.

Pulmonary tuberculosis stands first among all causes of death in women of childbearing age. In England and Wales, in 1936, respiratory tuberculosis accounted for 25 per cent of all deaths in females of the age group 15–44 years. This is 3 times as many as deaths due to puerperal causes of all kinds.

It is difficult to assess the incidence of phthisis in association with pregnancy, for as yet there is little information available on this point. Browne[20] stated that 82 cases of phthisis had been encountered among a total of 16,000 pregnancies observed at University College Hospital from 1928 to 1937 (incidence 0.51 per cent). Brindeau *et al.*[14] reported a total of 254 cases among 32,667 pregnant women admitted to the Tarnier Clinic during a 10-year period (incidence 0.77 per cent). Bridgeman and Norwood[21] reported 134 cases in 14,000 parturient records from the Johns Hopkins Hospital, Baltimore (incidence 0.96 per cent). None of these authors states the proportion of cases of active disease, and as their diagnostic standards may vary these figures are probably not strictly comparable. It is evident that the clinical examination made as part of the routine antenatal supervision at most maternity hospitals will reveal only a proportion of all cases of phthisis, and that if cases are not to be missed some form of radiological examination is essential. An investigation of this problem was begun at Paddington Hospital in 1943, and from that year a screen examination of the chest has been included as part of the routine for all women attending the antenatal department, as soon as possible after the first attendance.[22] In every case where screen examination shows possible pulmonary disease a full-size film is taken. From January 1943 to April 1946 a total of 4,430 women have been screened and the results are summarized in Table II.

Only one other survey of this type has been traced in the literature, that of Eisele *et al.*,[23] who carried out screen examination of the chest under rather similar conditions in a series of 10,968 women attending the antenatal department in a Chicago hospital during the years 1934–41. Table III summarizes the findings in all the above-mentioned series, together with those in a series of 59,951 W.A.A.F. recruits examined by miniature radiography (Trail *et al.*[24]), and some figures showing the number of new cases of phthisis discovered in women aged 15–45 years in 1937 in the County of London.

For various reasons it would be unwise to compare these figures too closely, as they may be influenced by unknown factors. Nevertheless, if we compare the results of the Paddington screening survey with those obtained by rather similar methods in Chicago, we see that we have to reckon with an incidence of probably more than 0.5 per cent of cases sufficiently severe to need immediate admission to hospital. Nearly 60,000 births occur annually in the

County of London, and approximately 10 times that number in England and Wales, and if these figures are capable of general application it becomes evident that a hospital problem of great magnitude is at present being avoided only by our failure to diagnose more than a small proportion of the existing cases. Only radiological methods are adequate for the discovery of the unsuspected cases, and the need for routine radiological examination of the chest in pregnant women appears to be at least as pressing as in those other groups of the population to which it is now being applied. Of the methods available miniature radiography would probably be the most satisfactory but there are at present certain difficulties in applying it. Until these are overcome screen examination could largely meet the need, and it has the advantage of being already available at most hospitals. Experience at Paddington Hospital has shown that it can be quite easily introduced, and that the co-operation of the mothers is very good.

TABLE II.

Screening Survey at Paddington Hospital.

Total number of pregnant women screened ...	4430	
Total number of patients radiographed	249	(5.70 per cent)
Cases of pulmonary tuberculosis:		
Active, requiring immediate admission ...	27	(0.61 per cent)
Possibly active	11	(0.25 per cent)
Probably inactive	30	(0.67 per cent)
Total cases of tuberculosis ... ... (Excluding calcified lesions)	68	(1.53 per cent)
Calcification shadows ... ... (Only large or multiple ones filmed)	39	
Non-tuberculous conditions, various	27	
Azygos vein lobe	10	(0.22 per cent)
Increased vascular shadows	34	

MANAGEMENT OF PREGNANCY IN TUBERCULOUS WOMEN.

Diagnosis of the many unsuspected cases is only the beginning of the problem. As indicated in Table III, an incidence of 0.5 per cent of severe active cases would mean a total of over 280 cases annually in the County of London alone, whereas at present the number of pregnant tuberculous women admitted to hospital from the L.C.C. area is probably not much more than 50 annually. The problem of providing sufficient beds for treatment of the cases discovered is a corollary of all mass radiological surveys, and in the case of pregnant women special difficulties arise, for skilled obstetric care must be available as well as skilled treatment for the lung disease. At present, in many parts of the country, arrangements for the care and treatment of pregnant women suffering from phthisis are inadequate even for the manifest cases, and pregnant women experience even more difficulty than others in obtaining prompt treatment. None the less, provisions for treatment can be made only when the full extent of the problem is revealed, and the wider use of radiological methods is urgently required. In addition to its advantages for the patients, it would create an admirable material for research into the effects of pregnancy upon phthisis, for the cases discovered would be unselected. Existing studies are mostly

based upon cases revealing themselves by symptoms, and a brief experience of radiological survey methods will soon convince anyone that these are an unrepresentative selection.

patients under treatment. The long period of in-patient treatment and separation from the child make many women reluctant to accept treatment at all. A determined effort must be made to mitigate the diffi-

TABLE III.
Incidence of Pulmonary Tuberculosis in Pregnancy.

Author etc.	Method of survey	Total women	Cases of phthisis	Per cent of total	Active phthisis per cent
Browne U.C.H. 1928–37	Clinical	16,000	82	0.50	?
Bridgeman Johns Hopkins Baltimore	Clinical	14,000	134	0.96	?
Brindeau Tarnier Hospital 10 years	Clinical	32,667	254	0.77	?
Eisele, *et al.* Chicago 1934–41	Screening	10,968	110	1.38	0.67
Jacobs Paddington 1943–46	Screening	4,430	68	1.53	0.61
General Incidence in Women of Child-bearing Age					
Trail, *et al.* W.A.A.F. 1941–44	Miniature radiography	59,951		0.94	0.36
L.C.C., 1937 Females 15–45 years	New cases phthisis diagnosed	1,071,000	2217	0.21	?
County of London, 1937, total births				56,875	
Cases of phthisis (assuming a rate of 0.50 per cent)				282	

Even with the provision of more beds in institutions suitable for the handling of pregnancy as well as the treatment of phthisis, in many cases social factors add greatly to the difficulties of bringing

culties arising in the home when the mother has to enter hospital. One form of help would be the provision, without financial burden, of domestic help in the home, as well as the necessary financial help to meet

the expenses which tuberculosis imposes and which bear so hardly on all but the wealthiest homes.

We are now in a position to lay down certain principles governing the management of a pregnant woman suffering from phthisis:

(1) *Therapeutic Abortion.*

This is of little help. There are a certain number of cases in which it is indicated, perhaps mainly on social grounds. It can be considered only in the first 3–4 months of pregnancy.

(2) *Treatment of the Lung Disease.*

Pregnancy is an added indication for the promptest application of all possible methods of treatment, especially effective collapse therapy, on the usual indications. This will help to guard the lung against the possible ill-effects of labour. Treatment must be continued after labour, its duration being governed by the usual considerations.

(3) *Obstetric Care.*

Skilled obstetric care must be provided, preferably in the same institution where the lung disease is to be treated.

(4) *Care of the Infant.*

The child usually has to be separated from the mother at birth. If no suitable relative is available to care for it, the child has to be admitted to an institution, either an ordinary residential nursery or a special "preventorium" of the type successfully developed in some Continental countries.

(5) *Help in the Patient's Home.*

Domestic help and financial assistance in the home must be provided where necessary, as well as the usual valuable supervision by health visitors.

How can these principles best be followed in practice? During recent years considerable attention has been devoted to the problem by some of the larger health authorities. In the L.C.C. area, most cases are admitted to Grove Park tuberculosis hospital and are transferred for obstetric care to the nearby Lewisham General Hospital, where a special department has been established for them in the maternity block. After delivery the patients are retransferred to Grove Park Hospital and in some cases subsequently to country sanatoria. The Essex County Council has organized a special obstetric unit for tuberculous women at Black Notley Sanatorium, so that they may remain in the same institution throughout their treatment. The infants are usually admitted to ordinary residential nurseries.

In the areas of the larger health authorities, such arrangements as these have hitherto proved adequate to deal with the relatively small numbers of cases discovered at the antenatal clinics and tuberculosis dispensaries. If radiological methods were generally applied in antenatal departments, however, it would become necessary greatly to extend these facilities. It is doubtful whether the situation could be met by an attempt to organize maternity units in sanatoria, for these are often situated far from hospital centres and the problem of providing them with specialist obstetric staff would be very great. Moreover, the difficulty of inducing pregnant women to go into hospital is increased if beds be offered in institutions far from their homes. The best answer to this problem would seem to lie in making use of the large general hospitals, which have both specialist medical staff and specialist obstetric staff available, and are situated within easy reach of most patient's homes. The cases could then be promptly admitted to hospital and receive all necessary treatment, being retained in the general hospital until well after the puerperium. Finally, when the tuberculous disease is satisfactorily controlled, they

could be transferred to country institutions for the more ambulant stages of their treatment. Throughout the more critical period of treatment, and during labour and puerperium, the patient would then be under the care of specialist medical and obstetric staff, and would also be within easy reach of her relatives. While the patient is in hospital the provision of domestic help in the home can help to set her mind at rest and make her more ready to accept treatment. After she returns home it is no less essential to spare her excessive domestic drudgery.

In conclusion, the importance of the social factor must again be emphasized. The home difficulties are not easy to overcome, but unless we can do this our best efforts in the dispensary, the hospital and the sanatorium are likely to be wasted.

Summary.

1. Current views of the effect of pregnancy upon pulmonary tuberculosis and the indications for therapeutic abortion are briefly discussed.

2. Figures are given showing the incidence of pulmonary tuberculosis in a series of 4,430 pregnant women, as revealed by screen examination.

3. The problems encountered in the management of pregnancy in tuberculous women are discussed and some principles for their solution enunciated.

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The Cause of Prolapsus Uteri in Women in the Light of Perineal Prolapse in Mice

BY

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THE condition about to be considered seems to be one of those many ailments whose aetiology in man can be elucidated by a study of their occurrence in lower animals.

Spontaneous prolapse of the uterus and vaginal perineum has occurred somewhat frequently among mice in this institution. The lesion has been specially investigated in our untreated 'Stock Breeders'. All these mice have been mated within their own group, though brother × sister mating has not been strictly maintained. Prolapse of the rectum is also seen occasionally in this stock and occurs in the male as well as in the female; but even in the female prolapse of the rectum occurs independently of vaginal and uterine prolapse, and the following remarks are confined to the latter condition.

Clinical experience has taught that prolapse of the perineum in women is a sequel to parturition, and the condition is attributed usually to laceration or overstretching of the pelvic tissues, the evil effects of these lesions being enhanced by gravity through the upright stance. Such lesions of the pelvic tissues in women, however, are purely conjectural and perhaps do not exist. In any event the abnormality as it is seen in our mice cannot be attributed to such alleged causes, for in them the prolapse depends neither on labour nor the upright stance, and is in fact associated with some degree of infertility. We have studied all our female 'Stock Breeders', numbering 547, which were born in the years 1943 and 1944 and lived for 6 months or longer; every one had cohabited with a male. Prolapse of the vaginal perineum was found in 48, or 8.6 per cent of these mice. The condition was not peculiar to advanced life; the earliest age at which it was recorded was 83 days, and the defect was noted in many instances between that age and 200 days. The general fertility in this particular stock of breeding mice has been small; even so, a total sterility was commoner in those which ultimately had prolapse than in those which remained free from this lesion, as shown below.

	Total	Number sterile	Per cent sterile
Mice with prolapse ...	48	33	68.7
Mice without prolapse	499	232	46.6

Furthermore, the mice which eventually showed prolapse, even though they were occasionally fertile in early life, bore fewer litters than the others.

	Total number of litters	Average number of litters per mouse
Mice with prolapse ...	19	0.39
Mice without prolapse	575	1.15

These figures indicate that the perineal defect was associated with an early onset of sterility and was not the effect of parturition.

When the condition is examined in the living mouse the earliest sign to be noticed is a slight patency of the vagina with a consequent exposure of a small glistening area of the anterior vaginal wall (Fig. 1). This condition may be noted at a stage before the other external signs of prolapse have become manifest as they are in Fig. 2. Postmortem examinations yield noteworthy information. On opening the abdomen an early sign is a sinking of the bladder and the lower ends of the uterine cornua below the brim of the pelvis, and it is remarkable that in every instance of the lesion, incipient or advanced, investigation has revealed an enlargement of the vagina (Fig. 3). It appears in fact that this vaginal enlargement has an important share in the etiology of the prolapse and probably is the initial defect.

Various incidental complications of the lesions have been noted, including hydronephrosis, abnormal distension of the uterus with clear fluid, and distension of the intestines; such complications may be the result of paresis, partial obstruction through kinking, or both factors combined.

Hypertrophy of the uterus with luteinization of the ovaries is common, and even though the mice have not littered, the symphysis pubis is apt to be mobile without obvious separation of the bones. Perhaps some of these concurrences may have been caused by the unnatural stimulation of the vaginal end of the uterus to which its prolapsed position makes it liable, for it has been shown by various authors that pseudopregnancy can be induced in animals by artificial stimulation of the cervix uteri.[1, 2, 3, 4, 5]

It has not been possible to attribute these cases of perineal prolapse in mice to a mendelian cause; they are distributed evenly throughout our stock, and obviously interfere with procreation.

The Bearing of these Notes on Human Pathology.

From these observations on mice an interesting point arises in connexion with human pathology. For it seems possible that in women, as in mice, chronic dilatation of the vagina with perineal prolapse may be the result, not of any initial laceration or stretching of the pelvic ligaments during labour as commonly thought, but to a failure of the vagina to involute completely afterward. If this be the case it is conceivable that our methods of treating the malformation may become modified; we may be able, indeed, to prevent its occurrence. To effect such a prophylaxis it will be necessary to watch the course of postparturitional involution of the vagina as shown by its size and muscular tone and to recognize a completion of the process.

Summary.

Prolapse of the vaginal perineum has occurred spontaneously in 8.6 per cent of our female 'Stock Breeders'. The condition is not a consequence of parturition; it is associated with infertility and its primary manifestation appears to be a persistent dilatation of the vagina. The abnormality in mice is believed to throw light on the aetiology of *prolapsus uteri* in women.

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FIG. 1.

Mouse 401. Early stage of prolapse in a sterile mouse aged 83 days. Condition verified by postmortem examination. Vagina enlarged, orifice slightly patulous, bladder below pelvic brim.

FIG. 2.

Mouse 400. Later stage of prolapse in a sterile mouse aged 119 days. Condition as in above except much more advanced. The uterus, especially the left cornu, was distended with clear fluid. Diameter of right horn 1.6 mm., of left horn 5.8 mm.

H.B.

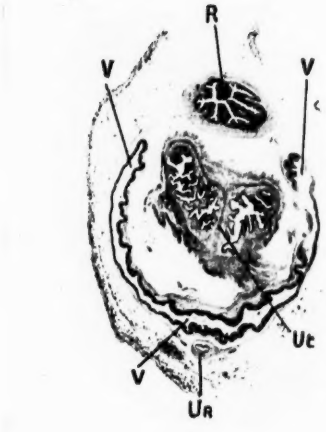

FIG. 3.

Mouse 406. Photograph of a coronal section of the prolapsed perineum in a sterile mouse of 169 days. The middle of the photo is occupied by the two united lower ends of the prolapsed uterus which are surrounded by a greatly dilated vagina. ×5

R. Rectum; Ut. Uterus; V. Vagina; Ur. Urethra.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.

A Meeting of the Council was held on Saturday, May 25th, 1946, in the College House, with the President, Mr. Eardley Holland in the Chair.

The following were formally admitted to the Fellowship by the President:

Arthur Capel Herbert Bell
John Lyle Cameron
Mabel Florence Potter
David Michael Stern

in absentia:

Edward Keelan
Newell Willard Philpott

The following were formally admitted to the membership by the President:

Constance Lang Beynon
Ernest William Cornwall Buckell
Walter Calvert
Raymond Gerard Cross
Gilbert Dalley
Perla Greeves
Emilie Ellen Guthmann
Werner Paul Hirsch
William Kearney
Arthur Harold Colyear Walker
Margaret Weddell

in absentia:

Sadashiv Narayan Garde

The Council acknowledged with grateful thanks a gift of £1,000 from Sir William Fletcher Shaw, to found a lectureship in memory of his son William Meredith Fletcher Shaw, who fell in Normandy in 1944, to be awarded annually to a senior Fellow of the College.

The Annual General Meeting of the College was held on Saturday, May 25th, 1946, in the College House, with the President, Mr. Eardley Holland, in the Chair.

The following were elected to Council in place of those retiring by statutory rotation:

Representative of the Fellows:

Robert Henry Mulhall Corbet
Arthur Alexander Gemmell
Arthur James McNair
Ernest Farquhar Murray

Representative of the Members:

Bryan Leslie Jeaffreson
James Sinclair Quin.

Professor Hilda Lloyd and Mr. L. C. Rivett were co-opted to the Council for special purposes.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

D.Obst. R.C.O.G.

Notice is hereby given that Regulation 3, relating to practitioners qualified over ten years, has been reinstated. Applications may be considered forthwith under that Regulation.

ROYAL SOCIETY OF MEDICINE

The Nichols Fellowship

Applications are invited for the above Fellowship, the emoluments of which are at the rate of £200 per annum and £25 for expenses.

The research is to relate to the aetiology, pathology, prevention or treatment of puerperal infection.

The applicants should give a précis of the proposed scope of the research and where it is to be carried out.

In the first instance the Fellowship shall be awarded for one year and may be continued for a second year after consideration of a report of the work already done.

Applications should reach the Secretary, Royal Society of Medicine, 1 Wimpole Street, London, W.1, on or before September 30th, 1946.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Postgraduate Medical School, Ducane Road, London, W.12.

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ANATOMY

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The Superiority of the South African Negro or Bantu as a Parturient

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PART I.—THE SIZE OF THE BANTU HEAD AT BIRTH.*

THE Bantu female pelvis has been compared with that of the Bantu male.[1] In comparing the female pelvic girdle of different racial groups, it is of value to know the relative size of the foetus for the respective races. For this reason an analysis of the gross birth-weight in over 2,000 cases was published;[2] but it is obvious that birth-weight would vary with good or poor nutrition during intrauterine life, probably in the main owing to the quantity of subcutaneous fat laid down in the foetus. While the mean Bantu weight was about $6\frac{3}{4}$ pounds, the mean in a smaller series receiving good antenatal care was $7\frac{1}{4}$ pounds, a near approach to the average for any prosperous European community. It is, therefore, of importance to assess the size of the head in the Bantu newborn, for this is the biggest part of the foetus to pass through the birth canal. The correlation table (Table I) demonstrates that in the newborn there is not a very marked relation between weight and the area of a cross-section in the plane of the occipito-frontal and biparietal diameters of the skull.

*This paper was presented as Appendix 3 of a D.Sc. Thesis submitted to the University of the Witwatersrand, South Africa.

Measurement was carried out on 500 heads of which two-thirds were Natal Zulu, one-fifth Basuto, and the rest Xhosa, Swazi, and Mpondo. Males and females were taken at random, and no separate analysis is shown for the sexes.

The birth-weight was observed in all cases, and on the day of birth the following head diameters were measured: the occipito-frontal, biparietal, suboccipito-bregmatic, and mentovertical. Areas were calculated to represent a cross-section of the greatest part, as it traverses the pelvis, of (*a*) the well-flexed head (biparietal and suboccipito-bregmatic as axes), and (*b*) the deflexed head (biparietal and occipito-frontal as axes). The correlation coefficient and regression equation for weight and area were calculated.

The measurements considered are those of the vault of the cranium, because the latter forms the major portion of the skull. In the full-time foetus the face, mandible, and temporal bones are small, the size of the head depending on the four large squamous bones, that is, the two parietal, the frontal, and the occipital.

Mean birth-weight. For 500 babies ranging in weight between 60 ounces (3 pounds, 12 ounces), and 178 ounces (11 pounds, 2 ounces), the mean weight was